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DIAGNOSIS OF CARDIOVASCULAR DISEASES BY GRAPHIC METHODS

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Diagnosis of cardiovascular diseases is reached by a complex process of reasoning based on the history of the patient, his present symptoms, his physical signs, and all the laboratory data including records obtained by graphic methods. The part played by the latter is far greater in this than in other fields of Internal Medicine.

The developments of the physical sciences and their technical applications, in particular electronics, have multiplied the number of graphic methods which can be used in the study of a cardiac patient. At the same time, they have so simplified the technic that a single operator, or at most a two-man team, can use these procedures.

Some of present day methods represent merely technical improvements over older ones, like electrocardiography which uses modern, direct writing, multiple lead electrocardiographs. Other methods are technically far superior to older ones, like present day electric recording of the arterial and venous pulses. On the other hand, other methods have no counterpart in older procedures. Among the latter are: cardiomanometry, which records the pressures of the cardiac chambers; phonocardiography, which registers the sounds and murmurs of the heart; ballistocardiography, which traces the movements of the body by effect of cardiac dynamics; and electrokymography, which registers the motions of the heart and vessels by means of the fluoroscope.

While clinical diagnosis of cardiac disease may reach a certain point of exactitude without graphic methods, use of the latter permits far greater accuracy, and greater certainty, in most of the cases. The following description summarizes briefly which methods should be preferred, as the most fruitful, in the various diseases of the cardiovascular system.

1—*RHEUMATIC HEART DISEASE*

(A) *Acute Rheumatic Fever*

As known, this disease is most frequent in infancy and childhood. Its diagnosis is often difficult because the symptoms and signs may be minor, vague, or atypical.

The *electrocardiogram* is frequently of help by revealing evidence of rheumatic carditis. It should be remembered that repeated electrocardiograms are even more important than one tracing alone because minor differences observed in successive tracings may indicate the evolution of an inflammatory process in the myocardium.

The following data should be considered as valuable:

(a) Evidence of disturbances of the

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heart rate (sinus tachycardia; severe sinus bradycardia ; severe sinus arrhythmia).

(b) Evidence of disturbances of the heart rhythm (atrial, nodal, or ventricular premature contractions; atrial or ventricular tachycardia: atrial flutter or fibrillation; a-v block and s-a block).

(c) Prolongation of the P-R and the Q-T intervals.

(d) Changes in the configuration of the P and T waves.

(e) Rapid and sudden change of the electric axis.

The *phonocardiogram* may be helpful for the evaluation of the auscultatory findings. Evidence of the existence of an apical or pulmonic systolic mumur, of a triple rhythm (gallop rhythm), of a split 2nd pulmonic sound, of prolongation of the 1st or 2nd sound, is important. In later stages, the existence of an opening snap of the mitral valve indicates a more severe lesion of this valve.

The *cardiogram* may be useful in order to ascertain the phase of any extra sound. It will help in deciding whether a triple rhythm is caused by an opening snap or a gallop sound.

The *electrokymogram* of the left atrium is useful in order to interpret the meaning of a systolic murmur. If there is evidence of a "systolic swelling" of the left atrium, an organic lesion of the mitral valve is likely.

Contributory evidence is secured by the determination of sedimentation rate and the accurate study of the graphs of weight, temperature, and pulse.

(B) *Mitral Valve Lesions*

The *electrocardiogram* may give evidence of either left or right axis deviation. The former is more consistent with a predominant insufficiency; the latter, with a predominant stenosis. Abnormal height, configuration, and duration of the P wave may be related to hypertrophy of the left atrium and damage to the atrial myocardium. An abnormally long P-R interval is not unusual and is caused by fibrosis of the conducting tissues resulting from carditis. Any disturbance of the rate or rhythm should be correlated with the functional conditions of the myocardium, the dilatation of the cardiac chambers, the action of drugs, etc. On the other hand, severe distention of the left atrium, favored by fibrosis of the atrial myocardium, may be one of the elements favoring the onset of atrial fibrillation. If a-v block is present, this is usually caused by a recurrence of rheumatic carditis. Evidence of either left or right ventricular hypertrophy or strain may be revealed by the ecg tracings in the various leads, especially by the chest leads. In mitral stenosis, the pattern of right intraventricular block or bundle branch block can be observed. The lesion is favored by right ventricular enlargement.

The *phonocardiogram* gives evidence of the existing murmurs. It reveals an apical systolic murmur "in decrescendo," typical of mitral regurgitation. It may show a triple rhythm due to the addition of a diastolic sound; this indicates some degree of ventricular strain. In mitral stenosis, any or all of several graphic phenomena may be observed: opening snap of the mitral valve in early diastole; split 2nd pulmonic sound; early or mid-diastolic rumble; presystolic murmur "in crescendo". Differential diagnosis between predominant insufficiency, predominant stenosis, combination of the two, or functional diastolic murmurs, is considerably helped by phonocardiography.

The *cardiogram,* a tracing of the low frequency vibrations of the precordium, and the *juglar tracing,* have mainly a contributory interest, in the sense that they may explain and "time" the various murmurs or sounds recorded by phonocardiography.

The *electrokymogram* of the left atrium reveals the existence of a typical, abnormal pattern. This consists of the transmission of ventricular pressure to the atrial chamber through the incompletely closed mitral valve. Thus, a tracing resembling the plateau-like tracing of ventricular pressure is recorded over the atrial border. This typical pattern is found, not only in cases with a loud

systolic murmur, but also in cases of so-called "pure" mitral stenosis with no systolic murmur. It proves the basic unity of the various types of mitral lesions. Recording of this pattern is fundamental for the differential diagnosis between the systolic murmur of mitral insufficiency and that of ventricular septal defect. On the other hand, a severe, functional regurgitation of the mitral valve might cause the appearance of the same pattern.

Contributory evidence may be secured by means of the various roentgenological methods, by the study of circulation time, etc.

(C) *Aortic Valve Lesions*

The *electrocardiogram* reveals a left axis deviation in both aortic insufficiency and aortic stenosis. Evidence of left ventricular hypertrophy, left ventricular strain, or both, may be found in the records of various leads, especially the chest leads. The existence of some impairment of the coronary circulation, caused by the valvular lesion, may also be found in these patients. The existence of intraventricular block or bundle branch block, usually of the left side, may be revealed by the tracings, as a result of left ventricular enlargement and of impairment of the coronary circulation.

The *phonocardiogram* gives evidence of the various murmurs; soft, high-pitched, early-diastolic aortic murmur in aortic regurgitation; harsh, loud, diamond-shaped aortic murmur in aortic stenosis. The frequently concomitant mitral lesion is revealed by the picture of the respective murmurs over the apex and midprecordium. If there is bundle branch block, a splitting of the second sound and a weakening and prolongation of the first, are noted over all areas. The *Austin Flint* murmur is a rare occurrence. Many of the aortic cases which simulate mitral stenosis upon auscultation, present a triple or quadruple rhythm in the phonocardiographic record. The real A.F. murmur is revealed by large and irregular vibrations which usually start some time after the opening of the mitral valve and which, therefore, are different from the vibrations of mitral stenosis (small, irregular vibrations starting immediately after mitral opening). Only rare cases simulate mitral stenosis even in the phonocardiogram.

The *apex cardiogram* may reveal typical patterns: high, peaked, dome-shaped tracing in aortic insufficiency; low, prolonged, frequently staggered tracing in aortic stenosis.

The *arterial tracings*, recorded at the suprasternal notch and over the subclavian or carotid arteries, again present typical patterns: a high, rapidly expanding, rapidly recoiling pulse in aortic insufficiency (*pulsus celer*); a low, slowly expanding, staggered pulse in aortic stenosis (*pulsus tardus, pulsus anacrotus*); the vibrations of the systolic thrill may be seen in the tracing of the latter (*carotid shudder*).

The *electrokymogram* may present interest if recorded over the left ventricular border and the aortic knob. In aortic insufficiency, the ventricular kymogram gives a pattern of rapid contraction in systole and of extremely rapid dilatation in early diastole (regurgitating blood enters the ventricle). The tracing of the aortic knob is similar to the carotid tracing. In aortic stenosis, the ventricular kymogram reveals a slow, staggered, contraction. The tracing of the aortic knob is similar to the carotid tracing.

Differential diagnosis between *aortic insufficiency* and *pulmonic insufficiency* is aided by the electrokymograms of tne two large arteries: a rapidly expanding and large pulse is found over the aortic arch in aortic insufficiency; over the pulmonic arch, in pulmonic insufficiency. Apart from the rare cases of organic pulmonic insufficiency, this problem becomes actual in cases of mitral stenosis with a *Graham-Steell murmur*. As the latter is caused by functional pulmonic insufficiency, the pulmonic arch presents the type of a high, rapidly expanding, and rapidly collapsing pulse (*pulsus celer*).

Differential diagnosis between *aortic stenosis* and *pulmonic stenosis* is aided by the electrokymogram of the two large arteries and the lungs. In pulmonic stenosis, a typical small pulse is found over

the pulmonic arch while the lungs reveal extremely small pulsations or none at all.

Differential diagnosis between the murmur of mitral stenosis and the *Austin Flint murmur* is aided by electrokymography. In mitral stenosis, a pattern of regurgitation of the mitral valve is constantly found over the left atrium. As the Austin Flint murmur is caused by a functional disturbance, no such pattern is found in cases with this murmur.

Graphic registration of the arterial pressure may be necessary in certain cases. It reveals a large pulse pressure and a low diastolic pressure, in aortic insufficiency; a small pulse pressure and a high diastolic pressure, in aortic stenosis.

(D) *Tricuspid Valve Lesions*

The *electrocardiogram* may reveal right axis deviation, right ventricular hypertrophy, right ventricular strain, or right bundle banch block, in tricuspid insufficiency with or without stenosis of this valve. The nearly constant association of mitral and tricuspid lesions may decrease the diagnostic value of these data. A high P wave has been described in tricuspid stenosis. However, these patients present an early onset of atrial fibrillation so that this finding may be impossible.

The *phonocardiogram* frequently indicates the existence of a systolic murmur "in decrescendo", a diastolic rumble, or both, over the tricuspid area. Differentiation from similar murmurs arising in the mitral valve is based on the observation that these murmurs become louder in inspiration in the case of tricuspid lesions; become less loud or persist unchanged in the case of mitral lesions.

The study of the low frequency vibrations of the chest and abdomen (*regional cardiograms, epigastric tracings*) may reveal the existence of a massive see-saw movement, so that the apical region is depressed in systole while the epigastrium and the high side of the chest have a violent forward thrust in the same phase. These motions are evident only if tricuspid insufficiency predominates.

The *jugular and hepatic tracings* present a high and peaked atrial wave if the sinus rhythm is preserved. This wave is of particular interest in cases with predominant tricuspid stenosis where diagnosis is more difficult. Tricuspid insufficiency is revealed by a high positive wave which assumes a plateau-like appearance if the lesion is severe. This wave is caused by transmission of right ventricular pressure to the right atrium and the venous system through the damaged tricuspid valve.

The *electrokymogram* of the right atrial border reveals typically a pattern of ventricular pressure, e.g. a rectangular positive wave instead of the normal systolic collapse. However, this wave is apparent only if the lesion is severe on account of the strong and direct pull exerted by the ventricular mass over the atrium.

2—*LUETIC HEART DISEASE*

(A) *Aortitis with Aortic Insufficiency*

The data supplied by the *electrocardiogram*, the *phonocardiogram*, the *aortic and carotid tracings*, and the *electrokymogram* of the aortic arch are similar to those found in rheumatic aortic regurgitation. They are useful for the differential diagnosis between the murmur of *aortitis* and that of *aortic stenosis*. The recognition of an Austin Flint murmur, as already said, is based on the phonocardiogram of the apex and the electrokymogram of the left atrium.

(B) *Aortic Aneurysms*

The diagnosis of location of aortic aneurysm is aided by comparison of several *pulse tracings* (right and left subclavian, right and left carotid, suprasternal and abdominal aortograms, etc.). These may indicate delay in the rise, and modification of the contour, of the pulse in the arteries below the aneurysm. The *electrokymogram* may be used in doubtful cases for the differential diagnosis between aortic aneurysms and mediastinal tumors. A densogram of an aneurysm reveals an arterial type of pulsation (unless the pouch is full of clots) while that of a tumor indicates small or non-existent pulsations.

In difficult cases, the differential diagnosis between the aneurysm of the pulmonary artery and that of the thoracic aorta may require *catheterization of the pulmonary artery.* The tip of the catheter enters the aneurysm, if this is pulmonic, and a tracing of its pressure is recorded.

3—*ATHEROSCLEROSIS—CALCIFIC AORTIC STENOSIS*

(A) *Aneurysm of the Abdominal Aorta*

This may be studied by means of *aortograms.* Two simultaneous mechanical tracings, taken from the opposite sides of the mass, indicate that this has an expansive pulsation (two positive pulses) while a tumor would show a transmitted pulsation (one positive, one negative pulse).

(B) *Dissecting Aneurysm*

This aneurysm may require comparison between radial pulse and abdominal or femoral tracing. In the dissecting aneurysim the femoral pulse is frequently smaller or disappears. Occasionally, decrease of the pulse of one or both subclavian arteries may also occur.

(C) *Calcific Aortic Stenosis*

The data supplied by the *electrocardiogram,* the *aortic* and *carotid tracings,* the *phonocardiogram* and the *electrokymogram* of the aortic arch are similar to those found in rheumatic aortic stenosis. They are useful in the differential diagnosis between the systolic murmur of aortic stenosis and that accompanying atherosclerosis of the aorta.

(D) *Atherosclerosis of the Aorta*

Fibrosis of the Cardiac Valves

Patients with atherosclerosis of the aorta and diffuse arteriosclerosis frequently present a systolic murmur. Graphic methods are of help in the correct evaluation of the latter.

The *phonocardiogram* helps to decide whether the murmur originates in the mitral or in the aortic valve. The former is of a "decrescendo" type; the latter has a diamond-shaped aspect. The former is recorded best at the apex; the latter, over the aortic area.

The *carotid tracing* helps in the evaluation of the aortic murmur. If this is caused by calcific aortic stenosis, the pulse has a typical aspect (see aortic stenosis). If the pulse curve is normal, slight irregularities or loss of elasticity of the leaflets, or dilatation of the ascending aorta (relative stenosis), explain the murmur.

The *electrokymogram* helps in the evaluation of the apical murmur. If the pattern obtained over the left atrial border is normal, the murmur is caused by fibrosis of the valve, unimportant in itself. If, on the other hand, a plateau-like tracing is obtained, the murmur is caused by regurgitation, and the patient has a scarring of the valve, most likely caused by rheumatic endocarditis.

If the abdominal aorta is affected, graphic tracings help in the evaluation of symptoms and signs. Abnormal *pulse tracing* of the abdominal aorta and abnormal *ballistocardiogram* may have some interest for the diagnosis. The former is particularly important in the atherosclerosis of the abdominal aorta and in the aneurysm of this vessel.

4—*HYPERTENSIVE HEART DISEASE*

The *electrocardiogram* of hypertensive patients has a certain importance in the evaluation of the severity of cardiac involvement. The patterns of left axis deviation, left ventricular hypertrophy and strain, myocardial ischemia, or bundle branch block, are revealed by the various leads and studied best by means of the unipolar limb and chest leads. Whenever the electrocardiogram fails to reveal hypertrophy and strain of the left ventricle, the term "hypertensive heart disease" is not justified.

The *phonocardiogram* indicates whether there is a triple rhythm and whether this is due to an additional diastolic sound (gallop sound) or to split 2nd sound (in cases of bundle branch block); it reveals the existence of apical or basal functional murmurs during systole. In cases with extreme enlargement of the left ventricle and "relative mitral stenosis" it reveals a diastolic rumble which may be differentiated from that of mitral stenosis because the former is very loud, tumultuous, and occurring some time after the opening of the mitral valve.

The *electrokymogram* of the left ventricle may indicate abnormalities of the left ventricular contraction and thus give evidence of myocardial damage.

A *tracing of blood pressure* is needed in certain cases with an *auscultatory gap*, where clinical readings are frequently misinterpreted.

A *pulse tracing* (carotid, subclavian, or brachial) may reveal the existence of *pulsus alternans*, a phenomenon having a serious prognostic meaning.

Ballistocardiography may reveal abnormal patterns which may have some value for prognosis.

Catheterization of the right heart has been done, so far, only for study purposes. It may be necessary, in certain cases, in order to ascertain the degree of suffering of the right ventricle and the extent of pulmonic hypertension.

Repeated studies by means of phonocardiography, electrokymography, sphygmography, and electrocardiography may give evidence of improvement after a lumbodorsal sympathectomy, through gradual disappearance of the abnormal findings.

5—*CHRONIC COR PULMONALE*

The *electrocardiogram* of chronic lung patients has a certain importance in the recognition of a possible cardiac involvement and in the evaluation of its severity. The patterns of right axis deviation, right ventricular hypertrophy and strain, or bundle branch block, are revealed by the various leads, and especially by the unipolar limb and chest leads. The occurrence of a large P wave in leads 2 and 3 (P-pulmonale) may add contributory evidence to the diagnosis.

The *phonocardiogram* may reveal a triple rhythm, due to the addition of a diastolic sound (gallop) over the midprecordium and epigastrium. This would confirm the existence of right ventricular strain and stress. The finding of a systolic murmur over the pulmonary artery indicates distention of this vessel; that of a loud 2nd pulmonic sound, hypertension of the lesser circulation; that of a prolonged 2nd pulmonic sound followed by an early diastolic murmur, fibrosis of the pulmonic valve with pulmonic incompetence.

The *jugular* and *hepatic tracings* may reveal a high atrial wave indicating high pressure in the right atrium. If there is a positive wave in systole, the sign is evidence of severe right ventricular strain, dilatation of the right ventricle, and functional tricuspid insufficiency.

The *electrokymogram* of the right ventricle may indicate the severity of myocardial damage through abnormality of the contraction pattern. The kymogram of the hilar shadows and of the various lung fields may reveal the extent of impairment of the pulmonary circulation. High pulsations are usually found over the hila; small or absent pulsations, in those vascular districts which are mostly affected by fibrosis. In the case of an a-v fistula of the lungs, the pulmonary shadow presents an expansive pulsation.

Catheterization of the right heart reveals the level of pressure in the various chambers, the extent of repercussion on the right ventricle, and the gradient between pulmonary artery and pulmonary "capillaries". If an increased gradient is found and this decreases after oxygen administration, there is vasoconstriction of the pulmonary arterioles caused by hypoxia and contributing to the hypertension. The possibility that treatment may influence this vasoconstriction shall be considered and the prognosis will somewhat improve.

Respiratory tracings may indicate whether an important bronchospastic component, revealed by prolonged duration of the expiratory phase, contributes to the dyspnea. *Spirograms* may indicate whether the vital capacity is severely impaired.

The various data supplied by cardiomanometry and by the electrocardiogram, phonocardiogram, electrokymogram, and the respiratory tracings, are very valuable for diagnosis and prognosis.

6—*CORONARY HEART DISEASE*

The *electrocardiogram* has the greatest importance in this field. Still, the inadequacy of this method in the borderline

cases and in some obscure clinical pictures indicates the need for functional tests and for resorting also to the data supplied by other graphic methods.

(A) *Angina Pectoris*

In cases of *angina pectoris* with normal electrocardiogram, the ecg study should be effected with the help of the unipolar limb leads, at least six unipolar chest leads, and the VE lead. The Master "two step" test and, in some cases, also the "anoxemia" test, may be needed. The *ballistocardiogram* may reveal an abnormal pattern which indicates abnormal left ventricular contraction due to the underlying coronary heart disease.

(B) *Myocardial Infarct*

In *myocardial infarct,* diagnosis is usually reached by means of the electrocardiogram in conjunction with the data supplied by history and with physical data. It should be kept in mind that repeated tracings are far more informative than one only because they demonstrate successive changes. Minor abnormalities sometimes assume a great importance if they follow a definite pattern and a well known type of evolution from day to day. The typical patterns of certain leads clearly reveal the location of the infarct.

The most revealing data are found in the chest leads V1 to V3 for the *antero-septal infarct;* in aVL, 1 and 2, and the chest leads V3 to V6, for the *antero-lateral infarct;* in aVF, 2 and 3, and the chest leads V5 to V7, for the *postero-lateral infarct;* in aVF, 3, VE, and the low esophageal leads, for the *postero-diaphragmatic infarct;* and in the high antero-lateral chest leads for the *high antero-lateral infarcts.*

The *phonocardiogram* may reveal the existence of a systolic murmur over the apex or the pulmonary artery, indicating dilatation of the left ventricle and hypertension in the lesser circulation; it may reveal extreme reduction in amplitude and pitch of the first sound, typical of an infarct; it may explain the curious auscultatory findings caused by the triple or quadruple rhythms (addition of one or two loud, but low-pitched, diastolic sounds); these are favored by tachycardia, high left atrial pressure, and a flabby and dilated left ventricular wall. The tracing may reveal the existence of loud systolic murmurs caused by rupture of the ventricular septum, or a chorda tendinea, or formation of an aneurysm in the wall of the left ventricle.

The *pulse tracings* (carotid, subclavian, brachial) may reveal the existence of *pulsus alternans,* a phenomenon which implies a severe prognosis.

The *jugular tracing* may reveal data indicating high pressure in the right heart due to heart failure.

Following the acute stage, the extent of myocardial damage may be evaluated by means of the following methods:

(a) The *electrocardiogram* may reveal bundle branch block, intraventricular block, disturbances of the rate and rhythm, and continuing evidence of severe myocardial ischemia.

(b) The *phonocardiogram* and *pulse tracings* may reveal continued evidence of triple rhythm, weak heart sounds, functional murmurs, and pulsus alternans.

(c) The *electrokymogram* of the left ventricle may reveal several important data. The first is the existence of a limited area of non-contracting muscle surrounded by normally contracting tissues (*local paralysis*). The second is the existence of an area presenting an inverted type of pulsation (*paradoxical pulsation*); this has a definite meaning if it assumes a rectangular pattern similar to that of intraventricular pressure (*dynamic aneurysm*) and more so if there is no permanent bulge. Further, it may reveal minor abnormalties, or a normal pattern of contraction. It is apparent that the last two eventualities, and especially the last, are consistent with limited myocardial damage and indicate a better prognosis.

(C) *Myocardial Fibrosis*

Several patients with coronary heart disease have no acute episodes of infarc-

tion (or these are not witnessed by physicians) and have no anginal pain. The gradual reduction of efficiency of the myocardium is revealed by the *electrocardiogram* and especially by the functional electrocardiographic tests (evidence of coronary heart disease; decreased tolerance to exercise; by the *phonocardiogram* (triple rhythm, functional murmurs); by the *electrokymogram* (abnormal left ventricular contraction); and by the *ballistocardiogram* (small waves, abnormal pattern). Further data will be given below.

7—*MYOCARDIAL DISEASES*

(A) *Acute Myocarditis*

Acute and subacute myocarditis are accompanied by severe changes of the *electrocardiogram*. Changes of the P and T waves, abnormalities of the QRS complex, evidence of disturbances of the rate and rhythm, changes of the P-R and Q-T intervals, have diagnostic value.

The *phonocardiogram* may reveal weakening or prolongation of the first sound, functional murmurs or triple rhythm.

The *pulse tracing* may show the existence of a pulsus alternans.

The *electrokymogram* may reveal abnormal ventricular patterns.

(B) *Subacute Myocarditis*

In *subacute myocarditis,* bundle branch block and intraventricular block are common. The *electrocardiogram* is frequently able to tell whether or not such a disturbance is present and which side is affected. The chest leads are particularly helpful. However, it should not be forgotten that a possible ventricular asynchronism due to bundle branch block is easily detected in the following ways:

(a) By comparing the phonocardiogram with the carotid and jugular tracings. These reveal a delayed arterial pulse in left bundle branch block; a delayed *v* wave in right bundle branch block. A split 2nd pulmonic sound is present in both.

(b) By comparing the phonocardiogram with the electrokymograms of the pulmonary and aortic arches. A delayed aortic pulse is often present in left bundle branch block; a delayed pulmonic pulse in right bundle branch block.

It should be kept in mind, however, that hypertension of the systemic circulation tends to increase certain effects of a left bundle branch block (delayed opening of the aortic valve), to counteract those of a right bundle branch block. On the contrary, hypertension of the lesser circulation tends to cause the opposite effect. However, such a delayed opening of a valve (difficulty in overcoming the pressure of the artery) is accompanied by an earlier closure (effect of the high pressure) so that the tracing should permit recognition of this fact which sometimes tends to confuse the data.

8—*PERICARDIAL DISEASES*

The *electrocardiogram* may be useful in the diagnosis of acute and subacute pericarditis even if there is little or no effusion. The tracing frequently presents a typical pattern caused by lesion of the subepicardial layers of the heart. This consists of upward displacement of the S-T tract and late inversion of the T wave in all limb and chest leads. Even if somewhat resembling the pattern caused by myocardial infarct, the lack of coving, the lack of Q, and the different evolution, help in the differential diagnosis.

The *phonocardiogram* may reveal the existence of *friction rubs* in the acute stage; of an *early-diastolic snap or click,* in the constrictive form; of a *systolic snap,* in certain limited pleuro-pericardial adhesions.

The *electrokymogram* may be useful in the forms with effusion because the pulsations of the atrial and ventricular borders are smaller or absent while that of the aorta is normal or only slightly duced in amplitude. In constrictive pericarditis, a typical V-pattern reveals the impairment of diastolic filling.

Both the *arterial* and the *venous* tracings may be of interest; they may reveal an inspiratory engorgement of the veins with an extreme reduction of the arterial pulse (Kussmaul phenomenon). This abnormality is typical of adhesive

pericarditis but may be found in certain cases with effusion.

Cardiomanometry should be used before undertaking surgery in the cases with constricted pericardium. It indicates where the most important effects are felt: high pressure in the veins and not in the right atrium is found in cases with pericaval obstruction; high pressure in the right ventricle indicates that the left heart is compressed. A typical atrial and ventricular pattern indicates the difficult diastole of the right heart.

9—*CONGENITAL HEART DISEASES*

The *electrocardiogram* reveals right axis deviation, and frequently also right bundle branch block, in atrial septal defect, pulmonic stenosis, tetralogy of Fallot, and Eisenmenger complex; left axis deviation, in patent ductus arteriosus, tricuspid atresia or insufficiency plus shunts, coarctation of the aorta, aortic stenosis, and common arterial trunk. It may reveal a long P-R interval or a complete a-v block either as an isolated abnormality or in cases with ventricular septal defect. It shows a typical "coronary" pattern in the abnormal development of the coronary arteries.

The *phonocardiogram* shows a tracing which has diagnostic importance in patent ductus arteriosus; a late systolic and early diastolic murmur riding over the 2nd sound. Cases with tetralogy of Fallot frequently have a systolic murmur over the base and an early systolic snap at the right of the sternum. In both aortic and pulmonic stenosis, a loud, diamond-shaped, systolic type of murmur is noted. Also, the 2nd sound is weak or absent respectively over the aortic or pulmonic area. In most of the other cases, the pattern of the tracing is not typical indicating a *nondescript systolic murmur*. However, more systematic studies in cases with a definite diagnosis should be made.

Cardiomanometry has the greatest value but its data should be compared with those supplied by cardio-oximetry and angio-cardiography. The finding of a high pressure (and a high content of oxygen) in the right atrium, right ventricle, or pulmonary artery, contributes to the respective diagnosis of atrial septal defect, ventricular septal defect, or patent ductus arteriosus. Typical data are obtained in cases with riding aorta and in other complex malformations. Low pulmonic pressure is found in pulmonic stenosis.

Electrokymography reveals absence of arterial pulsations in the lungs of patients with pulmonic stenosis; large pulsations of the pulmonary knob and hila in most conditions associated with high pulmonic pressure, like atrial septal defect, patent ductus arteriosus, and Eisenmenger complex. In patent ductus arteriosus, a high dicrotic wave is found in the pulmonic and often also in the hilar tracings. It indicates a sudden decrease of pulsations below the left subclavian artery, in cases with coarctation of the aorta.

Comparative *pulse tracings* (subclavian, femoral) are important for the diagnosis of coarctation. This abnormality is accompanied by a delay of pulsations and a small or absent pulse in the femoral arteries.

10—*ENDOCRINE, NUTRITIONAL AND METABOLIC HEART DISEASES*

In these conditions, one frequently tries to ascertain whether or not the heart is affected by an existing disturbance of the metabolism, a vitamin deficiency, or an anemia.

The *electrocardiogram* is frequently normal or moderately changed. This finding may contribute to the diagnosis through the exclusion of myocarditis, pericarditis, coronary heart disease, etc.

The *electrokymogram* may reveal abnormalities of ventricular contractions; it may exclude pericardial effusion.

Venous pressure tracings and *circulation time tests*, graphically recorded, may indicate the degree of venous engorgement and the rapidity of circulation. As known, the latter is increased in hyperthyroidism, beri-beri heart, and anemia; it is decreased in hypothyroidism.

The *phonocardiogram* may exclude valvular lesions and reveal *atypical murmurs* or a triple rhythm, evidence of functional disturbances.

11—*DISTURBANCES OF THE RATE AND RHYTHM*

The importance of the *electrocardiogram* for the diagnosis of the various types of tachycardia, bradycardia, and arrhythmia is so well known that its emphasis is superfluous. Still, it should be kept in mind that several types of disturbances of the rate and rhythm were described following studies of *jugular* and *carotid tracings* and before the existence of electrocardiography.

Certain cases present special problems and require a complete graphic study.

(a) Differential diagnosis between *atrial flutter* and *impure atrial fibrillation*.. The jugular tracing and the electrokymogram of either atrial border reveal sharply defined and regular atrial waves in cases of flutter. The phonocardiogram may also reveal atrial sounds. The electrocardiogram reveals atrial waves best in V1 or V2, where the exploring electrode is near the right atrium.

(b) Cases of *a-v block* may require a complete graphic study. High atrial waves are found in the jugular tracing, in the apex cardiogram, and in the epigastric and esophageal tracings. The electrokymogram of either atrial border also reveals well defined atrial waves. The phonocardiogram frequently reveals atrial sounds.

(c) In cases of *premature beats* the finding of atrial waves in the esophageal electrocardiogram at the atrial level may clarify auscultatory data. The study of the phonocardiogram, arteriogram, and phlebogram, may contribute to the recognition of the site of origin of ventricular premature beats. Intracardiac electrocardiograms may be resorted to in particularly difficult cases.

12—*PERIPHERAL VASCULAR DISEASES*

The study of patients with peripheral vascular diseases may be aided by graphic methods. Plethysmography and photoplethymography of the limbs; sectional records of pressure and pulses; sectional records of oxymetry and temperature, are of help in the determination of the severity, extension, and level, of any occlusive process. Together with roentgenological techniques, they help to reach a decision about surgery of the limb. Typical changes are found in arteriosclerosis of the extremities where *pulse tracings, plethysmograms,* and *ballistocardiograms* should be studied systematically.

13—*HYPOTENSION—SHOCK*

In these conditions, the study of the arterial and venous circulations is of great importance. Graphic determination of mean arterial pressure and pulse pressure, as well as that of venous pressure, are of help and may contribute to the safe use of various therapeutic measure including drugs and transfusions.

14—*HEART FAILURE*

In heart failure, one of the problems to be considered is what part of the clinical picture of congestion is caused by weakness of the heart muscle and what part is the direct effect of lesion of one or more of the valvular orifices. An accurate structural diagnosis, aided by graphic tracings (see heading 1), is therefore of help in this evaluation.

A second problem is that of excluding possible components caused by vitamin deficiency, anemia, or hyperthyroidism; here again graphic studies are of help (see heading 10).

A third problem is the evaluation of the extent of myocardial damage caused by previous myocarditis or by coronary heart disease. The use of graphic methods in such cases has been discussed already (see headings 6 and 7).

If there is hypertension of the greater or the lesser circulation, several graphic data may help in the evaluation of the severity of the functional disorder and its repercussions on the heart (see headings 4 and 5).

The part played by failure of the right or left ventricle may be evaluated in the following way:

(a) *Electrocardiogram.* Finding of a

right or left ventricular strain not justified by hypertension of the greater or lesser circulations, or by valvular lesions.

(b) *Phonocardiogram.* Finding of a triple rhythm at the apex (left ventricle) or at the epigastrium (right ventricle); of a systolic murmur at the apex (mitral), over the xiphoid (tricuspid), or over the pulmonic area (pulmonary valve) The first indicates dilatation of the left ventricle; the second, pulmonary engorgement and dilatation of the pulmonary artery; the third, dilatation of the right ventricle.

(c) *Cardiomanometry.* It may reveal increase of pressure in the pulmonary artery or right ventricle. If not justified by structural lesions, this indicates *left ventricular failure.* On the other hand, increase *of diastolic pressure in the right ventricle* is evidence of *right ventricular failure.*

(d) *Radiocardiography.* This tracing reveals that the radioactive matreial remains in the ventricular chambers much longer than usual. This is evidence of increase of the residual blood left within the ventricles at the end of systole.

(e) *Tracings of venous pressures.* Even though venous hypertension is now considered as due to venous hypertonus, which is only indirectly connected with the failure of the heart, the level of venous pressure in the same individual case is usually proportional to the severity of the failure.

(f) *Electrokymography.* It indicates the abnormalities of ventricular and atrial contractions.

(g) *Respiratory tracings.* Indicate repercussions of the failure on the respiratory center and severity of engorgement of the pulmonary vessels.

In conclusion, several clinical data, including the history, should lead to formulation of a series of problems. The graphic data frequently help in their solution and greatly contribute to an accurate diagnosis, a well established therapy, and a well grounded prognosis.

SUMMARY

The study of a cardiac patient includes the use of several graphic methods. Data supplied by the electrocardiograph, the phonocardiograph, the electrokymograph, and various other methods, are briefly presented for each type of cardiovascular disease.

MORPHOLOGY OF THE STELLATE CELLS OF KUPFFER

HANS ELIAS, Ph.D.*

When Knisely, Bloch and Warner stated in 1948 that phagocytes in the sinusoids of transilluminated frog livers were integral parts of their walls, that they did not have processes which bridged the lumina of the sinusoids, that they did not resemble spiders sitting across the vessels, that all cells lining the liver sinusoids were basically alike, and that they all were potential phagocytes, they aroused much opposition.

It will not be necessary to repeat in detail Knisely, Bloch and Warner's arguments for their opinion. Suffice it to say that they have demonstrated in motion pictures blood flowing rapidly through the sinusoids, with a velocity great enough to be unthinkable were there obstacles in its way.

Today, a controversy rages about this argument, not in printed publications, but during discussions. Knisely's school rejects the concept of the spider-like Kupffer cells, saying that they are artifacts of fixation. Many histologists and pathologists, however, believe in the demonstrability of spider-like Kupffer cells in fixed slides. This group does not accept the verdict "artifact" for the spider-like Kupffer cells.

In view of this controversy it seems necessary to re-examine the subject of the Kupffer cell from a morphological aspect. It will be necessary to remember the relation of the sinusoids to the liver parenchyma. It has been shown (Elias '49) that the liver is a continuous mass of hepatic cells tunneled by the continuous hepatic labyrinth, a network of lacunae. The lacunae are spaces in the wallwork of the hepatic parenchyma. The network of the sinusoids is suspended in the labyrinth of the lacunae. It is important to realize that the lacuna is not identical with the sinusoid. It is as little identical with it as is the lacuna in cartilage identical with the chondriocyte that lies in it. As a chondriocyte, the sinusoid may fill the lacuna, or it may not fill it. If it does not fill the lacuna, the sinusoid is surrounded by the perisinusoidal space of Disse. This arrangement is illustrated in Figure 1. For the present discussion it will not be necessary to consider the reticular network that surrounds the sinusoid.

If one reviews the literature, he finds that very few authors have given support to the opinion that the Kupffer cells bridge the sinusoids. We may call this opinion the "spider theory". Zimmerman ('23) and Pfuhl ('23) originated it. The former called the Kupffer cells "endocytes". Later only one investigator (Wolf-Heidegger '41) has given emphasis to this viewpoint. Nevertheless, it has become a generally accepted belief. The reason for the acceptance of the spider theory is disregard of the fact that the histological slide is only a thin slice of a three dimensional organ. It is important, however, to know what the investigators thought of the stellate cells of Kupffer.

In 1876 C. Kupffer reported, in a letter to Waldeyer (which letter was published in the Archiv fur mikroskopische Anatomie), on the existence of stellate cells surrounding the blood capillaries in the liver. These cells can be impregnated selectively with gold chloride. Kupffer noticed that the stellate cells are always found in intimate contact with the capillary wall. He believed that they were perivascular elements, that they did not belong to the capillary wall. (He stated that occasionally a process of a stellate cell may penetrate between two liver cells and that it may even establish contact with a bile canaliculus. In his later paper he said that these processes only appeared intercellular due to tangential cutting of adjacent liver cells. He no longer upheld his belief in their contact with bile capillaries.)

In 1899, Kupffer published a longer paper richly illustrated. He corrected his

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previous opinion concerning the perivascular position of the stellate cells and demonstrated clearly that they are integral components of the capillary wall. They may appear triangular or stellate depending on the direction of sectioning. According to v. Kupffer (1899), the wall of the sinusoid consists of a basal membrane (Grundlamelle) which carries the stellate cells. The processes of each stellate cell (fig. 1,A) are continuous with those of their neighbors. Kupffer was unable to impregnate cell boundaries in the sinusoid wall with silver nitrate injected into the portal vein, in spite of the clear demonstration of the cell limits in the endothelium of the interlobular and central veins in the same specimens. He, therefore, intimated that the sinusoid wall may be a synplasm (syncytium or plasmodium). The gold impregnated stellate figures do not have sharp outlines. It may, therefore, appear that they are only thickenings of the "Grundlamelle"; in other words that this basal membrane belongs to the stellate cells, as the interdigital web belongs to the frog's foot.

Kupffer did not demonstrate any other kind of cells in the wall of the sinusoids. Maximow (1928), however, thinks that there may be other cells in that wall. The authors of textbooks (William Bloom in Maximow and Bloom and Giuseppe Levi (1946) for example) have emphasized differences in appearance of the nuclei. According to Knisely, Bloch and Warner, these differences in nuclear structure are but expressions of temporary functional states.

Basically, Maximow ('28) and Mann ('28) accepted Kupffer's concept of the stellate cells as integral components of the sinusoid wall, separating the blood from the liver cells, and bulging into the lumen (see fig. 1,B).

Only Zimmermann ('23), Pfuhl ('23), and Wolf-Heidegger among the original investigators thought of the Kupffer cells as "endocytes" which are sitting entirely within the sinusoids.

Pfuhl ('23) describes the walls of the sinusoids as consisting of reticular fibers, a non-cellular basal membrane and pericytes. The Kupffer cells were thought to sit upon this wall internally. It appears to the reader that this statement of Pfuhl is not supported by sufficient evidence. Pfuhl states that the Kupffer cells may detach themselves from the wall, still adhering to it with one or several processes.

Zimmermann, the other exponent of the spider theory, goes a step further by affirming that the sinusoid wall consists of ordinary endothelium, while all the Kupffer cells are endocytes that stick with their processes to that wall. Wolf-Heidegger's paper will be discussed below.

Knisely, Bloch and Warner consider the spider-like Kupffer cells as artifacts of fixation and their existence in microtome sections as evidence that the classical histological method has little value.

This brief review of the scanty literature already shows that even the method of traditional histology gives little support to the spider theory. And the following analysis will show that the spider-like Kupffer cells are not artifacts of fixation but artifacts of interpretation.

If one considers the sinusoid as a little structure of three dimensions, it will become evident that even a perfectly preserved sinusoid, when sectioned, can offer aspects that may mislead.

Zimmermann's statement that he has observed Kupffer cells entirely surrounded by blood is easily explained. The body of the Kupffer cells protrudes into the lumen (fig. 1,A and B). It is about 10 microns in height. A section 5 microns thick or thinner parallel to the longitudinal axis of the sinusoid can cut off a slice of the bulging portion of a Kupffer cell, containing a section of the nucleus. And this slice will be surrounded by slices of blood cells. The section is geometrically comparable to a horizontal section through the cumulus oophorus, containing a slice of the oocyte and of the corona radiata surrounded on all sides by liquor folliculi. No connection with the stratum granu-

losum is seen. But it is known that it is attached, in a different plane, to the stratum granulosum of the follicle, even though it appears in the section as if the egg with its corona radiata were floating freely in the liquor folliculi.

Tangential sections of the sinusoid wall or thick sections including the entire sinusoid may show a Kupffer cell nucleus located in the middle of a lacuna. To interpret sections of this kind, it must be remembered that the sinusoid is not identical with the lacuna in which it is suspended. Thus, if one wishes to prove that a cell is located within a sinusoid he has to demonstrate the walls of the sinusoid between the cell in question and the liver cells. However, one sees Kupffer cells within lacunae, not within sinusoids. An intermediate, endothelial wall between them and the liver cells cannot be demonstrated.

Frequently, the Kupffer cells appear stellate even in routine hematoxylin and eosin sections. And they appear indeed freely suspended in a lumen and attached to the walls with a few processes. Such pictures are the result of shrinkage of the sinusoids. The reasons for such shrinkage have been pointed out by Popper ('48) and by Knisely, Bloch and Warner. It is the result of increased permeability of the sinusoid wall during states of anoxia. In this case, plasma seeps through the walls and fills the perisinusoidal spaces of Disse. We are dealing, then, not with an artifact of fixation but with a physiological condition which occurs in the agonal phase preceding natural death (Popper '48) and also during health as a temporary phenomenon necessary for the production of lymph (Knisely, Bloch and Warner '48).

This anoxic condition of the sinusoids with enlarged Disse spaces is illustrated in figure 1,C. Since the sinusoids remain attached to the liver cells at a few places (probably by means of reticular fibers), the spider-like appearance is produced.

It was material of this kind which Wolf-Heidegger ('41) used for his studies. He used the liver of adrenalectomized rats, just because he had an abundance of well fixed material. His illustrations show sinusoids in an extreme state of collapse surrounded by large Disse spaces. The sinusoids are attached to liver cells at some places. In addition to a great number of excellent microscopic drawings and photographs, he presents two diagrams which are the best evidence for the interpretation presented here: large, stellate structures containing a nucleus are shown sitting across the lacunae, touching the liver cells with their processes. No intervening endothelium is shown. Wolf-Heidegger states in the text that the plasmodial endothelium surrounds his allegedly stellate cells. But neither his thorough drawings and photomicrographs, nor his schematical diagrams show this surrounding endothelium. However, his presumed stellate cells are surrounded by erythrocytes. It is not astonishing that, in animals which have undergone such a severe mutilation as adrenalectomy, hemorrhages into the Disse spaces should have occurred.

In conclusion, it may be stated that the stellate cells of Kupffer, due to their position within the walls of the sinusoids frequently present in sections an appearance of sitting across a lumen. This lumen, however, is not the sinusoid but the hepatic lacuna (a part of the hepatic labyrinth) in which the sinusoid is suspended. In reality, the Kupffer cells are integral components of the sinusoid wall itself. Their processes are only thickenings of the wall and located entirely within this wall.

SUMMARY

The prevailing opinion that the phagocytes in the liver are sitting across the lumina of the sinusoids is shown to have resulted from a neglect of three-dimensional analysis of histological sections. In reality the liver phagocytes are integral components of the sinusoid wall itself. They are located entirely within this wall. Neither the cells nor their processes bridge the lumina of the sinusoids.

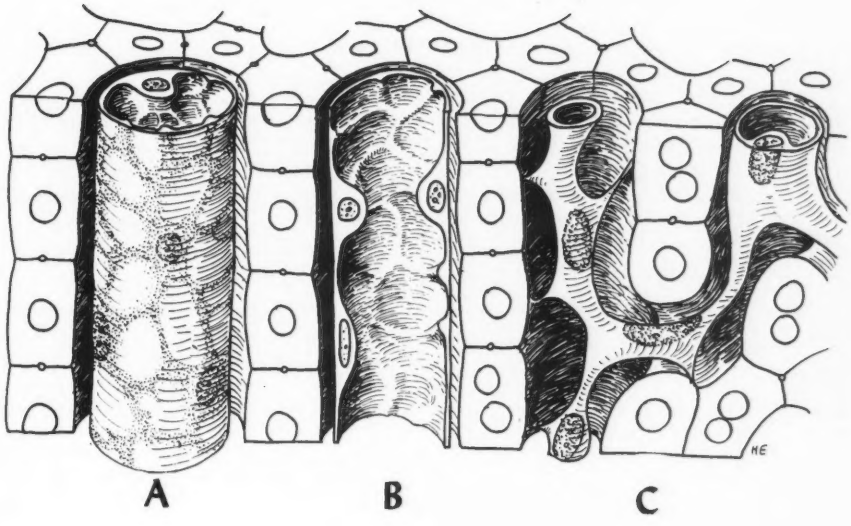

Fig. 1. Stereogram showing the suspension of the sinusoids in the hepatic lacuna. The sinusoid is surrounded by the perisinusoidal space of Disse which appears in states of anoxia because of increased permeability of the sinusoid wall. A and B: Slight anoxia; C: greater anoxia with shrinkage of the sinusoids. The Kupffer cells are components of the sinusoid wall and located entirely within the wall.

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COMMON SCROTAL ENLARGEMENTS

By DAVID PRESMAN, M.D.*

Enlargements of the scrotum occur relatively frequently and are often seen first by the general practitioner or internist. Because of the exposed position of the scrotum an accurate examination of its structures should be a simple matter and a diagnosis of the specific pathology causing the enlargement should present no particular difficulties. In addition, since there are but a few structures within the scrotum the number of pathological lesions is necessarily limited. In spite of these facts, the differential diagnosis of scrotal enlargements often presents a confusing picture to many physicians. If the anatomy of the scrotal contents and the known common causes of scrotal enlargement are kept in mind, an exact diagnosis should be made in most cases.

A carefully taken history will enable the examiner to eliminate certain conditions and reduce the diagnosis to one of several possibilities. The important specific facts which should be determined in the history are:

(1) Onset of swelling—acute or gradual.
(2) Duration of the swelling.
(3) Presence or absence of pain.
(4) Preceding trauma.

After these facts have been ascertained, a careful examination of the scrotal contents should yield a definite diagnosis. It is to be emphasized that the examiner must palpate for specific structures within the scrotum and not just casually feel an obviously enlarged mass. Many clinicians attempt to feel only the testis but this organ is the least common site of pathology within the scrotum. The other structures which should be carefully and specifically examined are the head and tail of the epididymis, the tunica vaginalis testis, the vas deferens, the supporting structures of the spermatic cord and the external inguinal ring.

It has been our experience that the best clinical approach to the diagnosis of scrotal enlargements is based upon the presence or absence of associated pain as determined in the history. The common causes of scrotal enlargement will be considered from this aspect.

PAINLESS ENLARGEMENTS

1. *Hydrocele*

This refers to an abnormal accumulation of fluid between the visceral and parietal layers of the tunica vaginalis testis. It is usually unilocular and in most cases unilateral. The chemical nature of hydrocele fluid is that of a transudate containing proteins, its composition being similar to blood serum. It is always yellow or straw colored in appearance.

A. *Congenital Hydrocele.* This occurs in infants and children and is due to failure of the processus vaginalis of the peritoneum to obliterate during the descent of the testes. As a result there is a communication between the peritoneal cavity and the two layers of the tunica vaginalis. Most hydroceles present in the newborn will disappear spontaneously within a few weeks. A congenital hernia may be associated with the hydrocele if the communication with the peritoneal cavity is large enough to permit omentum or intestines to pass through. Some congenital hydroceles may persist for periods varying from several months to a few years and then disappear due to obliteration of the open processes vaginalis and absorption of the hydrocele fluid. Others do not subside spontaneously and require operative repair.

B. *Primary or Idiopathic Hydrocele.* This is the commonest type of hydrocele and is usually seen in the middle and older age groups. The etiology is not definitely known but most cases are probably secondary to a low-grade, subclinical, non-specific epididymitis. The onset is gradual and the enlargement is painless. It may be present for many years without causing any appreciable discomfort but a large hydrocele may

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produce a dragging sensation because of its weight. There is no history of preceding trauma or inflammation.

Physical examination reveals a smooth, globular or pear-shaped mass which is firm and non-tender. The size is variable and with time may progress to that of a football. The testis often cannot be palpated if the amount of fluid is large. With smaller hydroceles, the testis may be felt at the lower posterior portion of the mass. The upper border of the hydrocele is limited at the inguinal ring and the spermatic cord can be felt just above the hydrocele. Some degree of fluctuation may be elicited depending upon the tension of the fluid within the hydrocele sac. As a rule, the hydrocele will transilluminate light unless the wall of the sac has become markedly fibrotic and thickened, as occurs in long-standing cases.

C. *Secondary or Acquired Hydrocele.* A hydrocele may be secondary to trauma or other disease processes within the scrotal cavity. The common lesions causing secondary hydrocele are tumor of the testis, acute non-specific epididymitis, chronic tuberculous epididymitis and mumps orchitis. The formation of the hydrocele may be acute or chronic depending upon the nature of the underlying lesion. The possibility of a coexisting testicular tumor should always be considered in the presence of a hydrocele in the young adult. In these patients, if the testis cannot be adequately palpated because of the hydrocele fluid, aspiration of the fluid or surgical removal of the hydrocele sac is indicated to evaluate the condition of the testis. Direct trauma to the scrotum may be followed by acute hydrocele which usually becomes absorbed after a short period of time. Trauma to the blood vessels of the spermatic cord or interference with the circulation during hernia repair or varicocele operations may also be followed by a hydrocele.

The treatment of hydrocele consists of aspiration of the fluid with a needle and syringe or surgical removal of the hydrocele sac. Aspiration is a temporary measure since the fluid always reaccumulates within a short time. Aspiration followed by the injection of sclerosing solutions is not recommended because of the severe pain and extensive sclerosis and damage to the testis which may ensue. The only satisfactory cure of a hydrocele is surgery: either removal of the sac or eversion of the cut edges around the testis and spermatic cord.

2. *Spermatocele*

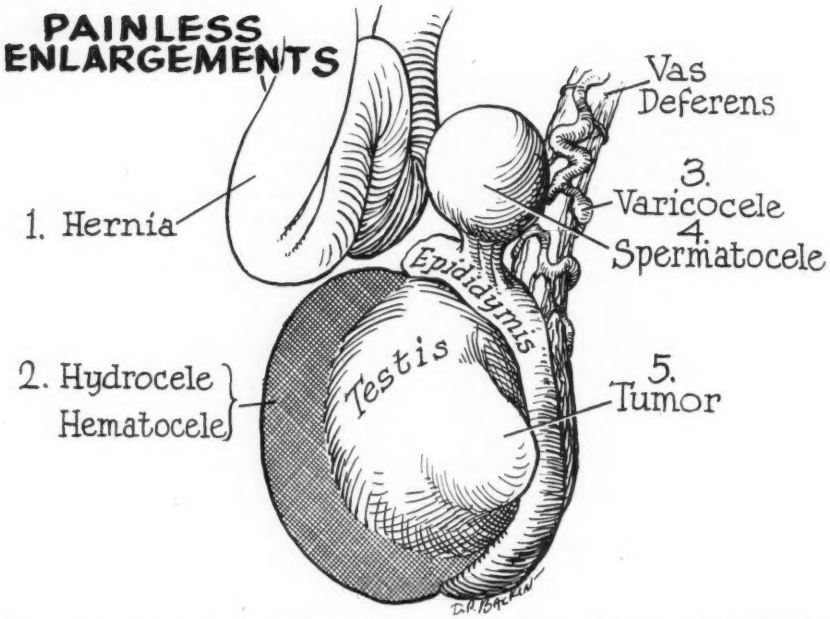
A spermatocele is a retention cyst which develops from a blind-ending aberrant vas efferens in the head of the epididymis. It may also arise from a normal vas efferens which becomes obstructed during late adult life. The secretions and spermatozoa produced in the testis gradually accumulate with a resultant dilatation of the involved vas efferens and the formation of a spermatocele cyst. Almost all spermatoceles are extravaginal, i.e., outside the tunica vaginalis testis.

Spermatoceles actually occur more commonly than hydroceles but many are not discovered because of their small size. They are usually overlooked by the patient until they become as large or larger than the testis. As a rule they are asymptomatic but the larger cysts may cause some degree of discomfort. Spermatoceles are commonly seen in the middle and older age groups but small ones may be found in young adults upon a careful examination of the scrotum.

The characteristic finding is that of a cystic mass located just above the testis and seemingly attached to the upper pole of the testis. It may be misdiagnosed as a supernumerary testis. Some degree of fluctuation is always present and the mass transilluminates light as does a hydrocele. The fluid of a spermatocele is never yellow or amber but is always clear or slightly turbid. This is due to the presence of spermatozoa which may be seen on microscopic examination.

The only definitive treatment of spermatocele is surgical excision. The entire cyst must be removed in order to prevent a recurrence. Aspiration of the contents is invariably followed by reaccumulation of the fluid.

3. *Hematocele.* This is an accumula-

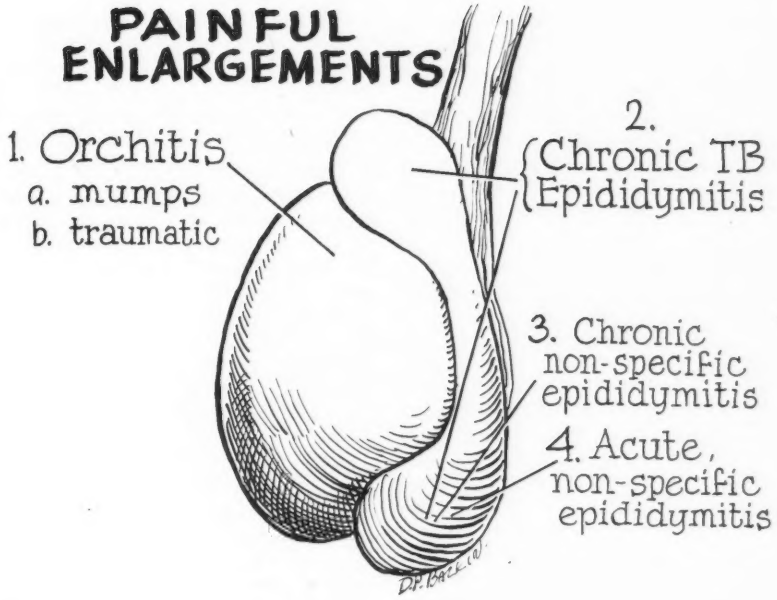


tion of blood between the layers of the tunica vaginalis testis resulting from direct trauma to the scrotum. It may also form following injury to a pre-existing hydrocele with resultant bleeding into the hydrocele sac. Its appearance and consistency resembles a hydrocele but it will not transilluminate light. The overlaying skin is often tense and shiny. The hematocele may be painful initially due to the sudden distension of the tunica vaginalis but the pain rapidly subsides. The blood may gradually become absorbed or it may persist with partial organization. With persistence of the mass, operative removal of the entire hematocele sac may be necessary to effect a cure. This condition differs from a hematoma of the scrotum which is a subcutaneous collection of blood following trauma and is limited to the scrotal wall.

4. *Varicocele.* This consists of a mass of varicose veins of the pampiniform plexus of the spermatic cord. It occurs practically always on the left side presumably because the left internal spermatic vein drains at right angles into the left renal vein. The right spermatic vein joins the vena cava at only a slight angle with less back pressure.

The presence of a mass of worm-like configuration along the left spermatic cord above the testis is diagnostic of varicocele. The mass is apparent when the patient stands and largely disappears with the patient in the recumbent position. Most varicoceles are painless but some degree of discomfort may be present. Some type of scrotal support is sufficient to relieve the symptoms in these patients. It may be difficult to evaluate the symptomatology because of the functional factor which is often present. Operative intervention should be considered only as a last resort since symptoms may persist even after surgical removal of the varicocele.

5. *Hernia.* Scrotal hernias are especially common among older men. They may become very large, but most are painless and cause no real difficulty. The hernial mass is usually firm and somewhat irregular depending upon the amount of omentum within the hernial



sac. The mass will feel soft and fluctuant if bowel is present and there is usually a definite impulse palpable on coughing. A scrotal hernia lies above or in front of the testis and in front of the spermatic cord.

If the mass is reducible the diagnosis is obvious. However, an incarcerated hernia may be confused with a hydrocele or a spermatocele. In most cases a scrotal hernia will not transilluminate light. Bowel activity may be felt on palpation of the mass or bowel sounds may be heard upon auscultation through a stethoscope. The differential diagnosis from hydrocele is important because of the danger of puncturing bowel if aspiration is performed.

6. *Tumor of the Testis*

Although this condition is relatively uncommon, it should always be considered in the diagnosis of scrotal enlargement in young adults because of its seriousness. Benign neoplasms of the testis are so rare that all testicular tumors must be considered malignant until proven otherwise.

The classification of tumors of the testis is based upon the predominant histological pattern: seminoma, embryonal carcinoma, teratoma, or teratocarcinoma (Friedman and Moore). Metastases occur via the lymphatics of the spermatic cord to the periaortic and retroperitoneal lymph nodes or by the blood stream to the lungs. Extensive involvement of the pelvic lymph nodes may lead to obstruction of the vena cava with peripheral edema or pressure on the nerve roots with intractable pain.

The patient usually seeks medical attention because of the discovery of a painless mass in the scrotum. Careful examination of the scrotal contents reveals a stony hard, movable, irregular mass limited to the testis. The epididymis and spermatic cord are normal to palpation and are not involved in the mass. However, it may be extremely difficult to differentiate a chronically thickened tail of the epididymis from an early testicular tumor of the lower pole. A secondary hydrocele may be present and obscure the exact localization of the mass. If testicular tumor is at all sus-

pected, the hydrocele should be aspirated or surgically explored in order to properly examine the testis. Determination of the gonadotropic hormone of the anterior pituitary in the urine (Ascheim-Zondek test) is of limited value. This test is positive only in a small percentage of cases, usually in the later stages of the more malignant tumors (chorioepitheliomas), so that a negative result offers no aid in diagnosis.

In some instances, the presenting complaints may be due to the metastases rather than the primary tumor. Vague abdominal pain, edema of the lower extremities, or enlargement of the abdomen may be the result of extensive involvement of the pelvic lymph nodes. Persistent cough may be the sole complaint due to pulmonary metastases. All cases of suspected testicular tumor should have a routine chest x-ray.

Treatment is surgical and consists of complete removal of the testis, epididymis and spermatic cord up to the inguinal ring. Post-operative irradiation to the abdomen and chest for possible metastases is recommended.

PAINFUL ENLARGEMENTS

1. *Acute Non-Specific Epididymitis*

This is a rather common condition and occurs among adult males of all age groups. In most instances the infection in the epididymis is secondary to infection in the seminal vesicles, prostate, or posterior urethra. The infecting organisms reach the epididymis as a result of retrograde extension along the vas deferens from the primary source. Any urethral manipulation such as passing a catheter, sound, or cystoscope may be a predisposing factor in the development of epididymitis. This condition may follow any type of surgical procedure on the prostate and should always be watched for during the postoperative period. Occasionally, epididymitis may be the result of hematogenous spread from a source elsewhere in the body such as an upper respiratory infection. The offending organisms usually are the common pathogenic bacteria such as staphylococcus, streptococcus, or any of the gram negative coli group.

With modern therapy of gonorrheal urethritis, gonorrheal epididymitis has become a rarity. Before the advent of the antibiotics the gonococcus was the commonest cause of epididymitis. Today it accounts for only a rare case of infection in the epididymis.

The term erotic epididymitis refers to a non-infectious inflammation of the epididymis which occurs following ungratified sexual excitement. The tail of the epididymis is only slightly enlarged and becomes painful and exquisitely tender. The probable cause is the retrograde regurgitation of the contents of the seminal vesicles through the vas to the tail of the epididymis because of failure of normal ejaculation. This condition is transient and usually subsides within twenty-four to forty-eight hours.

The history of acute non-specific epididymitis is usually typical. There is an acute onset of painful swelling in the scrotum. The pain may become very severe and is associated with malaise and fever. There may be a previous history of symptoms suggestive of prostatitis, seminal vesiculitis, or posterior urethritis. One should always question the patient specifically regarding any urethral instrumentation performed prior to the onset of the swelling.

Examination reveals an enlargement of one side of the scrotum which is hard, irregular and exquisitely tender. The overlying skin is warm, shiny and reddened. The mass varies in size but in most cases is as large as a baseball or larger. If the inflammatory reaction is very extensive it may be impossible to palpate any specific structure in the scrotum. As a rule, however, the hard irregular mass can be felt in the region of the tail of the epididymis. The testis may be involved secondarily but is usually unaffected. The spermatic cord often becomes indurated or edematous.

Torsion of the spermatic cord is a relatively rare condition but must be kept in mind inasmuch as it may simulate an acute epididymitis. Following any sudden movement or straining, the spermatic cord may twist so that the blood supply to the testis and epididymis is

obstructed. This results in an acute painful swelling with the rapid development of gangrene of these structures. The diagnosis is usually missed but can be made with a careful history and the palpation of an indurated mass involving the entire contents of the scrotum.

The treatment of acute epididymitis consists of bed rest, antibiotics, scrotal support, heat and fluids. The pain and fever respond rather quickly but the edema and induration may persist for several weeks. As a rule, the epididymis returns to normal without complications. In the elderly, debilitated patient, suppuration may occur with the formation of an abscess. In these cases, incision and drainage or epididymo-orchiectomy may be indicated.

2. *Acute Orchitis*

Inflammation of the testis is uncommon and occurs following trauma or secondary to mumps. A history of a direct blow to the scrotum followed by a painful swelling within a few hours suggests a traumatic orchitis. The testis becomes markedly painful and tender. There may be a secondary acute hydrocele which follows the initial inflammation. The orchitis and hydrocele usually subside with rest, elevation and heat without resultant sequellae.

Mumps orchitis is associated with or follows the typical parotitis. Involvement of the testis is more likely to occur in teen-agers or young adults. The testis becomes exquisitely painful and tender and there is associated fever and prostration. The swelling may persist for several weeks and in a large percentage of cases the testis becomes atrophied and sterile. Recent therapy aimed at rapid reduction of the orchitis to prevent atrophy has been reported with excellent results. The use of oral stilbesterol or incision of the tunica vaginalis and tunica albuginea to relieve the edema have been described.

It is to be emphasized that the testis is actually rarely responsible for enlargements within the scrotum. Approximately 95% of scrotal enlargements are due to pathology outside the testis proper.

3. *Chronic Non-Specific Epididymitis*

This causes a slightly painful enlargement of the epididymis with an insidious onset, developing and persisting over a period of months or even years. It may or may not follow an attack of acute epididymitis. Some discomfort in the groin or perineum may be present together with occasional mild urinary symptoms. This indicates the presence of an accompanying low-grade prostatitis or seminal vesiculitis which is usually the source of the epididymitis.

The tail of the epididymis is slightly enlarged, firm and irregular. Involvement of the head of the epididymis usually is associated with tuberculous infection. The vas deferens is normal to palpation. Massaged secretion from the prostate and seminal vesicles may show pus cells indicating a low-grade chronic infection. In most cases the symptoms of chronic epididymitis may be relieved by treating the associated prostatovesiculitis. The slight enlargement of the epididymis usually requires no further therapy unless the pain persists. For these occasional patients an epididymectomy is indicated.

4. *Chronic Tuberculous Epididymitis*

This condition has become less common in recent years with the decreased incidence of genito-urinary tuberculosis. However, it must be ruled out in every patient with a history of a persistent mass in the scrotum associated with some degree of pain or discomfort.

As a rule, tuberculous involvement of the epididymis is secondary to a primary focus elsewhere in the body, such as the lungs or kidneys. The spread is hematogenous in most cases and the epididymis is usually the first structure of the genital tract that becomes involved. The primary focus may be completely healed or it may be subclinical when the enlargement of the epididymis becomes apparent. However, inasmuch as definite activity of the primary lesion is demonstrable in approximately 50%

of cases, a careful search for the primary lesion should always be made. This should include a chest x-ray, sputum examination, smear, culture, and guinea pig inoculation of the urine for tubercle bacilli, and an intravenous pyelogram.

Tuberculous involvement of the vas deferens, prostate, and seminal vesicles may occur by direct extension from the epididymis. These structures, therefore, should be carefully examined in the presence of tuberculous epididymitis. In some instances tuberculosis of the genital tract is secondary to a primary lesion in the urinary tract. The infection may spread from the kidneys to the bladder and posterior urethra by urine containing tubercle bacilli. Further extension occurs from the posterior urethra involving the seminal vesicles, prostate and epididymis.

Tuberculous epididymitis initially involves either the head or tail of the epididymis. Caseation and multiple abscess formation occur at an early stage with gradual spread to the entire epididymis. The adjacent tissues such as the tunica vaginalis and scrotal skin become thickened and markedly adherent to the epididymis. The testis apparently has an immunity to the tubercle bacilli since it rarely becomes a part of the tuberculous process. With the formation of abscess cavities in the epididymis, one or more discharging sinuses form in the scrotal skin.

A history of *chronicity* in connection with a slightly painful scrotal mass is highly suggestive of tuberculous epididymitis. The presence of one or more draining sinuses in the scrotal skin is almost pathognomonic of this condition. In the early stages the enlargement of the epididymis may involve either the head or tail. Later the entire epididymis is enlarged but it rarely exceeds the size of a lemon. The mass is firm and irregular and is not part of the testis. The presence of a secondary hydrocele may interfere somewhat with a proper examination of the mass. Palpation of the scrotal vas reveals a diffuse thickening or a series of nodules along the course, the so-called "beading" of the vas which is characteristic of tuberculosis. Rectal examination of the prostate and seminal vesicles may demonstrate areas of nodularity or induration indicative of tuberculous infection.

In some cases of chronic epididymitis the differential diagnosis between nonspecific and tuberculous infection may be difficult and is made only on surgical exploration. The finding of localized areas of caseation in the epididymis will determine the diagnosis, but occasionally a microscopic examination of the excised epididymis is necessary to establish the true nature of the lesion.

The treatment of tuberculous epididymitis still remains surgical. Complete extirpation of the epididymis and vas deferens should be performed unless there is widespread tuberculosis throughout the body. It may be necessary to remove the testis in some cases because of marked adhesions to the epididymis, but, as a rule, the testis can be preserved. The use of streptomycin preoperatively is recommended because of its action in walling off abscess cavities and thus minimizing the spread of tubercle bacilli during surgery. Streptomycin in itself has not cured tuberculous epididymitis.

CONCLUSIONS

The diagnosis of scrotal enlargements should present no particular difficulty in most cases if the common pathological lesions occurring within the scrotum are kept in mind. A careful history paying special attention to the presence or absence of associated pain and the type of onset of the enlargement is of great value. Examination of the scrotum should include careful palpation of each specific structure in order to determine the exact nature and site of the lesion. Clinical experience has shown that the testes are the least common site of scrotal enlargements so that it is important to examine carefully *all* the structures within the scrotum in order to arrive at a correct diagnosis.

TWO YEARS OF ACTH AND CORTISONE THERAPY:

A REVIEW

By HUGO R. RONY, M.D.*

Author's Note:

The publication in April, 1949 of the paper of Dr. Hench and his collaborators on the effects of ACTH and Cortisone in rheumatoid arthritis provoked a great amount of experimental and clinical investigation designed to clarify the biological role and therapeutic value of these hormones. A veritable avalanche of reports has appeared in biological and medical journals during this brief period of time. The following review attempts to present the status of ACTH and Cortisone as it emerges at this time, the beginning of 1952. It is necessarily limited in scope: only the most important and most recent data are included, and theories, hypotheses and controversial views are omitted. More than 300 articles published in various journals in 1951 were reviewed. Acknowledgement is due to the Library of Armour Laboratories for the privilege of using its almost complete collection of reprints and abstracts concerning this subject.

CHEMISTRY

ACTH has been isolated as a crystalline protein which behaves as a single substance although its purity is subject to debate. Hydrolysis by pepsin and hydrochloric acid transforms it into a mixture of polypeptides—called ACTIDES—one or more of which retain the biologic effects of ACTH; the molecular weight of such an actide is of the order of 2000. ACTH contains no phosphorus, no carbohydrate or sulfhydryl groups.

BIOLOGICAL EFFECTS

Earlier data concerning the effects of ACTH and Cortisone on electrolyte balance, and protein, carbohydrate and fat metabolism have been confirmed and extended in 1951. In small dosage—as used in therapy to maintain relief that had been initiated by larger doses—these hormones have little or no effect upon the balances of Na, Cl, K, Ca or upon the concentration of these ions in the blood, even after long continued administration. Larger doses (100 mg. ACTH, 200 mg. Cortisone and up) frequently cause retention of Na and Cl, negative K balance, hypochloremic-hypokalemic alkalosis, negative N balance, increased excretion of urinary uric acid, occasional slight increase of blood sugar and decrease of sugar tolerance, occasional ketonuria, elevation in serum lipids including cholesterol, and osteoporosis. During prolonged high dosage therapy both hormones induce increased gonadotropin production regardless of sex or age. They induce depression of I^{131} uptake by the thyroid and decrease of protein-bound iodine in the serum with the gradual reduction in the basal metabolic rate, indicating inhibition of the pituitary thyrotropin production. The effect on blood coagulation remains uncertain: earlier reports that Cortisone causes hypercoagulability have been recently vigorously disputed. Cortisone inhibits the spreading of intradermally injected India ink enhanced by hyaluronidase in rabbits, rats and mice; also, it decreases the speed of absorption accelerated by hyaluronidase, through synovial membranes in joints of the rabbit. This may prove to be an outstanding effect of Cortisone—it may be instrumental in its effect on local inflammatory processes and rheumatoid arthritis. Both hormones in larger doses cause a sharp rise in the urinary excretion of ascorbic acid.

MORPHOLOGICAL EFFECTS

Earlier reports concerning the effects of these hormones on the thymus, spleen and lymph nodes in experimental animals have been confirmed. The lymphocyte count, in man, shows no uniform change; the drop in the number of circulating eosinophils following administration of either hormone remains the most reliable evidence of their activity. There is no decrease in the number of bone marrow eosinophils, which indicates that the effect on the blood eosinophils is probably due to an increased rate of removal from the blood without change in the production in the bone marrow.

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Cortisone inhibits growth of the chicken embryo and of the immature or young rat. It inhibits growth of premature human babies, although growth continues at normal rate immediately after cessation of administration. Cortisone on systemic as well as topical application inhibits hair growth in the rat. Under certain conditions it inhibits the growth of certain transplanted or chemically induced malignant tumors; however, the inhibition is temporary, and certain types of tumors do not respond at all.

Cortisone inhibits inflammatory reaction, fibroblastic proliferation, formation of collagen. Applied systemically or locally it inhibits granulation in wounds, interferes with wound healing. Reports are now available, on the basis of biopsies or autopsies, concerning histological changes brought about by ACTH or Cortisone administration in rheumatoid arthritis and other pathological conditions. Thus it was found that during systemic administration of either of the hormones there is prompt decrease in the number of total white cells and increased viscosity in the synovial fluid, in rheumatoid arthritis. On the other hand, subcutaneous nodules did not show consistent histological changes during therapy; neither were changes apparent in the histological picture of rheumatic carditis. Two patients suffering from periarteritis nodosa died in cardiorenal failure while treated with ACTH: autopsy showed complete healing of all arterial lesions, but in the process of healing fibrous obliteration of the lumens of the involved vessels occurred resulting in wide-spread visceral infarctions.

IMMUNOLOGICAL, ANTITOXIC AND ANTI-ALLERGIC EFFECTS

After earlier, somewhat controversial reports there is practically uniform agreement on the following data: The hormones have no effect on bacterial growth; there is no rise in circulating antibody levels in rabbits or rats injected with egg protein, pneumococcus vaccine, etc., and in man vaccinated with pneumococcal polysaccharides, while under treatment with Cortisone. On the other hand, the Schwartzman phenomenon is inhibited by ACTH or Cortisone if the hormone is administered within two hours of the provocative injection of the antigen; this is probably due to the local anti-inflammatory effects of the hormone. An analogous observation is made in rabbits intracutaneously injected with hemolytic streptococci: this results in fatal septicemia in Cortisone-treated rabbits, while the control animals develop but a slight cutaneous infection. This inflammatory reaction at the site of inoculation keeps the infection localized in the control animals, while Cortisone suppresses this reaction in the treated animals thus permitting the infection to become generalized. A similar mechanism seems to be operating in the effect of ACTH and Cortisone upon the resistance to tuberculosis. Administration of these hormones was found to be deleterious in at least three species of animals—mouse, guinea pig, rabbit—when infected with tubercle bacilli; and there is strong evidence of the same effect in man. On the whole, then, the hormones do not provide protection against bacterial infections, and may under certain conditions undermine our resistance to infections.

On the other hand, both hormones appear to exert a marked *antitoxic* effect in man as shown by the observation that in pneumonia and other infectious diseases as well as in non-infectious toxemias certain "toxic effects" such as fever, pain, loss of appetite, general malaise usually promptly disappear under hormonal treatment. No antitoxins have been demonstrated in the blood in such cases, and it is assumed that the hormone acts directly on the body cells by blockading them in some way against the toxin.

ACTH and Cortisone promptly alleviate allergic reactions; however, there is no change in the allergic state (skin sensitivity, etc.), soon after cessation of hormonal treatment. This can be explained in assuming that Cortisone blocks the effect of circulating allergens or allergen-antibody complexes upon the tissue cells.

UNTOWARD EFFECTS DURING THERAPY

The list of untoward effects—quite impressive since the very beginnings of ACTH therapy—is getting larger as more diseases in more patients are being treated. At the same time ways and means are found to avoid or minimize some of them.

The more common side effects are: edema, moon face, potassium deficiency, alkalosis, hypertension, glycosuria, abdominal striae, pigmentation, hypertrichosis, acne, amenorrhea, hypercholesterolemia, emotional instability, and the post-cortisone suppression syndrome (after hormone treatment is discontinued) manifested by anorexia, excessive weakness and fatigability. Rare but important untoward effects are thrombo-embolic complications, especially in persons with serious vascular disease or with history of previous thrombo-embolic disease; how ACTH or Cortisone brings about this complication is not clear. Spontaneous fractures were observed in a few cases; they are due to osteoporosis—a known possible effect of Cortisone, on prolonged administration. Bleeding from or perforation of pre-existing peptic ulcers had been reported while the patients were treated with Cortisone or ACTH, probably precipitated by the capacity of the hormone to inhibit fibroblastic proliferation and wound healing. Severe allergic reactions such as generalized urticaria, angioneurotic edema and shock have been observed in a few cases following intramuscular or intravenous injection of ACTH, especially at the start of a second series of injections, weeks or months after a first series was ended. This is remarkable in view of the fact that administration of ACTH in acute allergic states such as serum sickness, bronchial asthma, penicillin allergy etc. usually results in prompt termination of the attack. Allergy to ACTH may be species-specific, i.e. the patient may be hypersensitive to ACTH extracted from beef pituitaries but not hypersensitive to ACTH from pork pituitaries, or vice versa. In other cases the allergy to ACTH seemed to be pituitary—or ACTH—specific, rather than species specific. Another serious untoward effect is the development of real psychotic states, manic or depressive, in the course of hormonal therapy. This occurred with patients who were emotionally markedly unstable already before administration of the hormone or had a previous history of psychiatric disturbance. Finally, as mentioned before, rapid and progressive spread of lung tuberculosis during ACTH therapy was reported in some tubercular patients and in one patient who had no demonstrable tuberculosis before.

Masking of the signs and symptoms of a previous or intercurrent infection, while not an untoward effect of the hormone in the strict sense of the word, constitutes the greatest hazard of ACTH or Cortisone therapy. Such infections may be especially serious because they are not accompanied by fever and other toxic signs, and may get out of hand before recognized.

The frequency of the occurrence of untoward effects depends on the dosage of the hormone, on the duration of treatment, and on an individual factor, susceptibility of the patient. On prolonged treatment with larger doses as practiced earlier most patients developed some untoward effect. Recent statistics indicate occurrence of some side effect in 20 to 30 per cent of the patients. This improvement is due 1) to the recognition that in most cases small dosage of the hormone is capable of maintaining satisfactory remission of the disease, 2) to the prescription of a low sodium diet with added potasium chloride to all patients on higher hormone dosage, thereby preventing the commonest side effects, i.e. those due to electrolyte imbalance, and 3) to careful consideration of the contraindications to ACTH or Cortisone therapy with rejection of some cases and very cautious treatment of others. Fortunately, almost all side effects disappear without lasting harm soon after cessation of treatment or reduction of dosage.

CONTRAINDICATIONS TO ACTH, CORTISONE THERAPY

The following represents, at the present time, the list of contraindications,

from prohibitive to relative, in that order:

Active tuberculosis 1)
Cardiac failure
Psychopathic states and tendencies
Cushing's Syndrome
Severe diabetes 2)
Septicemia and other acute infectious diseases 3)
Thrombo-embolic manifestation or history thereof
Peptic ulcer
Decubitus ulcer
Coronary disease
Osteoporosis 4)
Hypertension
Hypertrichosis
Hypercholesterolemia
Acne

Ad 1): The National Tuberculosis Assn. recently advised that routine diagnostic examination, including chest film, for tuberculosis, be made *in all patients* who are being considered for ACTH or Cortisone therapy, that the hormone not be used in those with active tuberculosis, and used "with extreme caution" in those with possible latent tuberculosis.

Ad 2): Mild diabetes is not a prohibitive contra-indication. When treated with ACTH or Cortisone such patients should be kept on low carbohydrate diets and their insulin intake adjusted; they may need much more insulin than before. ACTH, Cortisone should not be used in the severe diabetic because of special danger of ketosis and electrolyte imbalance.

Ad 3): There is no complete agreement on this point. Some competent observers do not object to the use of ACTH or Cortisone in acute, severe, generalized infections such as pneumonia, or in acute localized infections such as peritonitis following rupture of the appendix, *provided the patient is simultaneously vigorously treated with antibiotics.* They find the hormones of great value to relieve the severe toxic signs and symptoms (high fever, great debility, pain etc.). More reports with more data will be necessary to decide this important question.

Ad 4): Osteoporosis is a contra-indication because of the danger that ACTH or Cortisone may accelerate the pre-existent osteoporosis and thus lead to spontaneous fractures. However, in case of urgent need for ACTH or Cortisone the bones may be protected by simultaneous administration of male and female sex hormone in adequate dosage. In most cases the final decision obviously must rest upon carefully weighing the degree of contra-indication against the need for the hormonal treatment in the individual case.

One other point of a different nature may enter the deliberation for or against administration of these agents: is the patient able to pay for the hormones over a prolonged period of time? As one observer writes: "One sees no unhappier individual than the patient with rheumatoid arthritis who has shown impressive response to therapy and who then relapses because of inability to purchase further medication. The addition of a flat pocketbook to his original disease represents no medical triumph."

It is evident that the list of contra-indications now is considerably longer than it was a year ago and it is a fair bet that further experience in the future will lead to further extension of the list.

TECHNIQUES OF THERAPY

ACTH—This hormone may be administered intramuscularly or intravenously. A newer preparation, ACTHAR GEL, a long acting repository product, is for intramuscular use only. For intravenous use 20 mg. ACTH is dissolved in 1000 cc. glucose solution and infused over 4 to 5 hours; it is claimed that the daily requirement of the hormone administered this way is but half of that given intramuscularly. With ACTHAR GEL, on the other hand, the whole 24 or 48 hour requirement of the hormone may be administered in one intramuscular injection. Very few reports are as yet available concerning the usefulness of ACTHAR GEL or of intravenously adminstered ACTH.

In regard to dosage most authors advise against the larger amounts used two

years ago. The usual adult initial dosage now is 60 to 80 mg. a day in divided doses, for a few days to a week, then gradual reduction to the maintenance dosage judged on the basis of the clinical status of the patient. In occasional cases —when the above mentioned dosage does not produce definite clinical improvement in 48 hours, and the drop in the number of circulating eosinophils is less than 50%—the initial dose may be doubled for a few days.

Cortisone.—This hormone may be administered orally or intramuscularly. It is now commonly used orally, except in the presence of gastrointestinal disturbances which might interfere with intestinal absorption of the hormone. Here, too, the tendency is to use smaller dosages than two years ago. Most authors report satisfactory results with 100 to 150 mg. daily by mouth, initially, followed by gradual reduction to 50 mg., the average daily maintenance dose.

No general statement can be made as to which of the two hormones is superior in therapeutic efficiency. Reports are available claiming superiority of ACTH in certain diseases, and superiority of Cortisone in other diseases. However, with the exception of acute gout—where almost all agree that ACTH is much more useful than Cortisone—and certain glandular conditions—where ACTH is useless or contraindicated while Cortisone is highly efficient—the reports are inconsistent. On the other hand, occasional patients suffering from the same kind of disease may respond favorably to ACTH and less so to Cortisone, or vice versa, indicating individual preference, the nature of which is not clear

Most patients respond quite equally to either hormone which is one reason why the *combined ACTH-Cortisone treatment* is becoming popular. The other reason is that in this way certain disadvantages inherent in the prolonged exclusive use of either hormone may be avoided. ACTH causes overactivity of the adrenal cortex with hyperplasia; Cortisone, by inhibiting the adrenocorticotropin production of the anterior pituitary, may cause atrophy of the adrenal cortex. Both effects may be abolished by simultaneous administration of both hormones in reduced dosage. In this combination—treatment the average initial dosage is 20 mg. ACTH plus 25 mg. Cortisone, twice a day; and the maintenance dosage is the same, once a day. Another recommended variation of therapy is to employ ACTH alone in the initial phase of treatment, then continue with combined ACTH and Cortisone in reduced dosage.

In an effort to avoid side effects by reducing dosage, attempts were made to combine ACTH or Cortisone with other hormones or drugs. Thus it is claimed that smaller doses of ACTH suffice to produce remission in rheumatoid arthritis when gold salts are used simultaneously. Pregnenolone, testoterone (to counteract the protein-catabolic effect of cortisone), other corticoids and ascorbic acid have been used in combination with ACTH or Cortisone, with variable results. Compound F (hydrocortisone) is now available in limited amounts for experimental therapy; there are indications that this corticoid alone or in combination with ACTH or Cortisone may lessen the hazards of therapy.

While earlier the initial phase of management in the hospital included such laboratory tests as the uric acid/creatinine ratio, 17-ketosteroids in the urine etc., recent reports indicate a tendency to simplify routine management. This begins with a careful history and examination, including a chest film, to recognize contraindications. Before the first administration of the hormone a count of circulating eosinophils is made. Then the following routine is observed:

1) body weight and blood pressure daily
2) fluid intake and output daily
3) circulating eosinophils every other day
4) fasting blood sugar twice weekly
5) sedimentation rate (if orig. high) twice weekly
6) limit sodium intake in the daily diet to 0.5 gm or less

7) add potassium chloride 2 gm. or more daily

8) daily protein intake 100 gm. or more

All observers emphasize the importance of the eosinophil counts as a practical indicator of hormonal effect; it does not consistently correlate with the clinical results.

A most important task of management, initially as well as later, is to watch for incidental infections which might easily elude attention because of the masking effect of the hormones, and to institute proper (antibiotic) treatment immediately if indicated.

It is still held that it is advisable to hospitalize all patients for the duration of the initial phase of treatment.

In rheumatoid arthritis and other chronic diseases cessation of hormone therapy is immediately followed by a relapse in most patients; in some, however, remission is maintained for weeks and even months. Therefore an attempt to temporarily discontinue administration of the hormone seems to be justified in all or most cases.

THERAPEUTIC INDICATIONS AND RESULTS

Recent experience has brought disappointments in the usefulness of ACTH and Cortisone in the therapy of some diseases and, as mentioned above, the list of contra-indications has become larger, but new uses for the hormones were discovered in other diseases. As a result the present list of diseases in which these agents can be usefully applied is probably longer than it was a year ago.

This list may be divided in two parts: I) conditions in which ACTH or Cortisone act as specific agents of therapy, and II) conditions in which they are used for their non-specific (blocking) action.

I. ACTH or CORTISONE as SPECIFIC AGENTS are indicated in

Panhypopituitarism

Addison's disease (Cortisone only)

Post-subtotal adrenalectomy (removal of adrenal tumors) (Cortisone only)

Post-total adrenalectomy (in some cases of cancer of the prostate) (Cortisone only)

Shock from burns, surgical operations or other causes

Idiopathic hypoglycemia

Functional (pituitary or hypothalamic) hypo-adrenocorticism

Status thymico-lymphaticus

The syndrome of functional hypo-adrenocorticism consists of weakness, fatigue, hypotension, minor hypoglycemia, emotional instability, and must be differentiated from psychoneurotic states. Status thymico-lymphaticus had been recognized years ago as a "constitutional anomaly," lost its identity later, and regained "status" recently as a form of adrenocortical hypoplasia.

Uniformly good results were observed in patients in these categories who received hormonal treatment, but the number so treated remains small at the present time.

II. ACTH and CORTISONE as NON-SPECIFIC AGENTS are being used in the therapy of a great variety of diseases. After overoptimism and some confusion in the first year of the "ACTH era" it is now well established that these hormones can be powerful and highly useful agents in the hands of the therapist who knows the indications and contraindications, the possibilities and limitations.

A) *Diseases requiring hormonal treatment for prolonged or indefinite periods of time*:

Rheumatoid arthritis

Sarcoidosis

Dermatomyositis

Pulmonary fibrosis

Disseminated Lupus Erythematosis

Pemphigus

Exfoliative dermatitis

Ulcerative colitis

Regional enteritis
Periarteritis nodosa
Scleroderma
Alopecia areata

Rheumatoid arthritis. Nearly 100% of these patients show subjective and objective improvement. There are now a number of patients on record who have been treated for two years or over with sustained improvement of the arthritis and without serious side effects. However, a few patients cannot long maintain a satisfactory remission because of the development sooner or later of refractoriness to the hormone or adverse side effects; combined ACTH-Cortisone therapy helped in some of these cases. Other "rheumatoid" diseases such as rheumatoid spondylitis, Still's disease, Felty's syndrome, psoriatic arthritis usually respond as well or nearly as well as rheumatoid arthritis. There is general agreement that patients with hypertrophic (degenerative osteoarthritis) arthritis are not helped by the hormones although according to recent reports marked benefits were observed in some cases of degenerative hip joint disease (malum coxae senilis).

Disseminated Lupus Erythematosus, Pemphigus, Exfoliative Dermatitis — marked initial improvement in almost all patients, but no complete clinical remission. Hormone treatment may be life saving and must be continued indefinitely.

Sarcoidosis, Dermatomyositis, pulmonary fibrosis (silicosis, beryllium granulomatosis, Loeffler's pneumonia)—almost uniformly favorable results.

Ulcerative Colitis, Regional enteritis— good clinical results in 60 to 70% of cases.

Periarteritis nodosa, Scleroderma — marked and prolonged remission in early phases of the disease. Little response in advanced stage.

Alopecia Areata—prompt regrowth of hair in 5 out of six cases, including alopecia areata totalis, was recently reported by a reliable observer.

B) *Diseases requiring hormonal treatment for short or limited periods of time.*

1. Acute or subacute infections and inflammations:
   Rheumatic fever
   Acute gout
   Periarthritis of the shoulder
   Shoulder-hand syndrome
   Reiter's syndrome
   Thyroiditis
   Cranial arteritis
   Iritis, keratitis, chorioretinitis, iridocyclitis
   Acute generalized peritonitis
   Trichinosis

Rheumatic fever.—Nearly all patients suffering from an initial attack respond with prompt remission to administration of ACTH or Cortisone in proper dosage. However, the duration of the disease is not shortened, and treatment must be continued until the natural termination of the attack, for four weeks or more. It is believed by most observers that a significant amount of cardiac damage may be prevented in this way. The hormones are now regarded to be superior to other means in the therapy of acute rheumatic fever.

Gout. — ACTH and Cortisone can promptly alleviate acute attacks of gout but are not superior to colchicine in this effect; however, they may be of special value in occasional cases where colchicine fails. They are of no value in the intercritical periods of chronic gout.

Periarthritis of the shoulder, shoulder-hand syndrome.—fair to good results in the majority of cases.

Reiter's syndrome, acute and subacute thyroiditis of unknown etiology, cranial (temporal) arteritis.—very good results in the few cases reported so far.

Iritis, keratitis, chorioretinitis, iridocyclitis—acute and sub-acute forms; almost uniformly excellent results according to all reports on many cases.

Acute, generalized peritonitis, due to ruptured appendix or other causes. ACTH or Cortisone added to chemotherapy, antibiotics and surgery improves

morbidity and mortality rates, according to some reports, by relieving shock and counteracting toxic effects.

Trichinosis.—Prompt relief of fever, muscle pain and other toxic effects in the stage when the larvae invade the blood and lymph stream. However, the larvae and cysts are not affected and the further course of the disease is not changed.

2. Allergic conditions:
   Atopic dermatitis
   Serum sickness
   Hay fever
   Bronchial asthma

Atopic dermatitis, Serum sickness.—Prompt relief of attack in almost all cases.

Hay fever. Favorable results by administration of Cortisone for the duration of the season. No change in reagin titer and no protection from next season's attack.

Bronchial asthma.—ACTH or Cortisone appear to be equal or superior to other means of therapy in terminating acute attacks of bronchial asthma or severe status asthmaticus. Treatment has to be continued for some time and dosage gradually reduced to prevent immediate relapse. According to some reports continued administration of the hormone in reduced dosage is capable to assure prolonged remission.

3. Blood Dyscrasias:
   Acquired hemolytic anemia
   Idiopathic thrombocytopenic purpura
   Henoch-Schoenlein purpura
   Hemophilia
   Agranulocytosis
   Acute (lymphatic) leukemia

Clinical improvement and favorable hematological response have been reported in a number of cases in each of these categories; exacerbations of the disease, attacks of hemolysis or of bleeding, toxic symptoms may be promptly relieved. Prolonged remissions may follow and, in acute leukemia, the fatal outcome may be delayed.

4. Other conditions:
   Alcoholism
   Toxemias of pregnancy
   Nephrosis
   Retrolental fibroplasia

Acute alcoholism.—There is general agreement that ACTH and Cortisone are very useful in the treatment of acute alcoholic states associated with stupor or with acute mania or delirium tremens. Complete recovery from such states may be accomplished in 24 hours with hormonal treatment, while otherwise it requires several days or more.

Toxemias of pregnancy.—Favorable results are reported in hyperemesis gravidarum and eclampsia.

Nephrosis. — All reports agree that ACTH or Cortisone may be very helpful in the treatment of nephrotic conditions: in the majority of patients diuresis follows with decrease of the edema and relief of toxic symptoms although the degree and duration of the remission is variable.

Retrolental fibroplasia in premature babies. Arrest and regression of the process were reported in a number of cases after a short course of ACTH injections.

ACTH and Cortisone have been employed in the therapy of many other diseases, with uncertain, indifferent or unfavorable results. It is not very likely that many more therapeutic uses for these hormones will be discovered; on the other hand, we can confidently expect further fruitful work concerning the mechanism of their actions on physiological and pathological processes.

CLINICOPATHOLOGIC CONFERENCE

Presented at Mount Sinai Hospital, Chicago, Ill.

Dr. N. I. Fox, Chairman, Dr. I. Davidsohn, Secretary.

Abstracted by Dr. A. Oyamada

This 51 year old white male entered Mount Sinai Hospital on June 19, 1950, as an emergency admission with a history of sudden onset of severe throbbing pain in the region of the neck. There was also severe dyspnea beginning abruptly about one and one-half hours previously. The pain radiated into the chest and was tearing and constricting in nature. The patient also stated that everything "went black" at the time. Within fifteen to twenty minutes, the pain radiated into the abdomen and was described as severe and throbbing. The patient had been seen by a physician and given morphine gr. ¼, atropine gr. 1/150, nitroglycerine gr. 1/100 and oxygen. On patient's entry into the ambulance his blood pressure was said to be normal but pulse was imperceptible. He had no previous history of hypertension, diabetes or organic heart disease. He had had a peptic ulcer for many years.

Physical examination revealed a well developed, well nourished, obese, white male, who appeared acutely ill. The patient was sitting in bed and was dyspneic with cyanosis of the lips and nail beds. The pupils were constricted and reacted to accommodation but only sluggishly to light. The chest was emphysematous with only a few coarse rales in the bases. Blood pressure was 130/80, pulse 80 and regular. The heart borders were not made out. At the apex, a systolic and early diastolic murmur were heard; also a rough systolic and early diastolic murmur were noted best at Erb's point and at the aortic region. The heart tones were distant. The patient was unable to move either lower extremity. Reflexes were absent on both lower extremities; no Babinski was elicited. The dorsal pedis and femoral pulses were good on the right leg, but were not felt on the left. The left foot was slightly colder than the right and definite cyanosis of the left foot was noted.

Hospital course: The patient was given positive pressure oxygen per mask. One hour after admission, the left foot was no longer cyanotic and was said to be warmer. At this time, the patient was able to move the toes of his right foot, though not of the left. As the first night went on, pulse was noted in the left leg in popliteal, posterior tibial, and finally dorsal pedis arteries (6½ hours after admission). At 9:00 A.M. on June 20th, the morning after admission, it was noted that the eyes were turned to the right. No nystagmus was present, but they could not be moved left past the midline. Pupils reacted as at admission. The tongue was in the midline, although by 1:00 P.M. the same day, it had deviated to the left with obliteration of the left nasolabial fold and drooping of the left corner of the mouth. By morning, the patient was able to move the toes on his left foot; however, motion of the left arm or leg was slight compared with the right side. Deep tendon reflexes were now present bilaterally. In fact, the patellar reflexes were somewhat exaggerated. No pathologic reflexes were noted except for some right leg clonus. The cremasteric reflex was absent on the left and present on the right; abdominal reflexes were absent. There was no evidence of sensory impairment.

The blood pressure was 90/60 at 1:00 P.M. on June 20th and temperature 101°. The patient was placed on penicillin, 400,000 U. daily. At 3:00 P.M. on June 20th, the blood pressure was 150/70 on the right arm and 160/65 on the left. By 5:30 A.M. the following morning, the patient was restless and complained of pain in the head. Blood pressure at this time was 160/60. At 4:45 P.M. on June 21st, the temperature was 102.6° rectally with a relative bradycardia. (There is no record of exact pulse.) The patient was perspiring freely; the skin was cold and moist. There was some tenderness in the L.L.Q. and bowel sounds were present but hypoactive. Blood pressure was 170/80.

LABORATORY DATA:

Bl. Count:	*RBC*	*WBC*	*Hb.*	*C.I.*	*Stab*	*Seg.*	*Eos*	*Lymph*	*Mono*
6/19/50	5.2	16.1	100%	.97	9	64	1	17	9

Urinalysis:	*S.G.*	*React.*	*WBC*	*RBC*	*Alb.*	*Sugar*	*Casts*
6/20/50	1.025	5.5	6-8	0	3+	0	12-15 granular
6/21/50	1.027	5.5	2-3	0	Tr.	0	3-5 hyaline & gran.

Bl. Chemistry:	*Sugar*	*Urea N.*	CO_2	*I.I.*	*VandenBergh*	*Chlor.*
6/20/50	109	16.8	49	6.8	Direct-0.19, Indir-0.9	97.8 mEq/L (N. 98-106) 572 mg% (N 570-620)

E.K.G. 6/19/50 — Normal E. K. G.
Sed. Rate: 6/20/50: 3 (corrected)
Hematocrit: 6/20/50 — 51
Prothrombin: Time 6/20/50: 14 seconds (control 12 sec.)
Clotting Activity: 68%
Serology: 6/21/50 — Negative

Over the course of the next day, the patient became comatose. He developed urinary incontinence, Cheyne-Stokes breathing and involuntary twitchings of the right arm and leg. Respirations were labored with loud audible rhonchi. The patient's condition deteriorated rapidly and he was found dead at 4:45 P.M. on June 22nd, slightly less than three days after the onset of his illness.

DISCUSSION OF CASE

Dr. W. Rothman: There isn't much more to add to the history of this case. The man was a clerk in a bank. He finished working at 8:05 P.M. when he had the attack with pain in the neck, cyanosis, and shortness of breath. When I was called I immediately got the Fire Dept. to give him oxygen. I gave the patient morphine and atropine by injection and nitroglycerine orally, and rushed him to the hospital. His blood pressure was 120/86 at the time of the attack. He had a systolic murmur. He had never had any previous attacks. I think he was intelligent enough to give a fairly good history of his condition. It was the first time I saw him. I had never treated the man prior to this occasion. As soon as he was brought into the hospital we were fortunate enough to get consultation. An electrocardiogram, taken at the hospital, was negative. We suspected a coronary disease.

Dr. E. B. Freilich: There were several factors we had to consider in the differential diagnosis. I happened to be here the evening when the patient was brought to the hospital. He was 51 years old, rather heavy set and well built, with no previous history of any cardiac trouble or abdominal disease. In view of the fact that he came in with this sudden onset of pain in the neck, chest, and abdomen, and loss of consciousness, the possibility first of all was a cerebrovascular accident, then an acute cardiac situation or an acute pulmonary embolism, or possibly acute gall bladder disease or pancreatitis. When he was first admitted I examined him with Dr. Getz and was impressed with the fact that he had migrating pains in the neck, chest, and abdomen. I considered two possibilities: 1) dissecting aneurysm and (2) coronary occlusion with myocardial infarction. The first electrocardiogram was negative. I got a later history from his family that he had had epigastric distress for a considerable length of time and an x-ray taken previously had shown no ulcer. I also learned from the family that he was a moderate hypertensive. When he was first taken ill, his blood pressure was 130. Then he went into shock and it dropped to 90, 80 etc. There was a diastolic murmur in the aortic area. The patient was married for a short time and then separated. There was the possibility of the aneurysm being luetic in origin. We had a Kahn test done, which was negative. As the case progressed, I became convinced then that we were dealing with a dissecting aneurysm of the aorta. The migrating pains which he had in the very beginning, the shock, and the diastolic murmur would very well fit in with a dis-

secting aneurysm. We had an x-ray taken which showed a widening of the mediastinum, which also was in accord with a diagnosis of dissecting aneurysm. The changes in the circulation in the lower extremities also would fit into the picture of a dissecting aneurysm, and that was my initial diagnosis and final diagnosis.

Dr. Kamen: The first electrocardiogram is essentially normal. The ST segments are isoelectric, the P waves are up, rhythm is normal sinus rhythm. In the next electrocardiogram, the first lead shows a tachycardia paroxysmal in character as we don't see it in any of the other graphs. This may be a supraventricular type. There is certainly no evidence of acute myocardial infarction. The other EKG's are essentially the same. There is no evidence of coronary disease as far as we can tell from the electrocardiograms.

Dr. J. Sterns: This is a portable film and only corroborates Dr. Freilich's diagnosis.

Dr. A. Luisada: The history of this case is so typical that one has to ask himself if there is some "catch" in it. I have the impression that it is a dissecting aneurysm of the aorta. The type of pain starting in the neck, radiating to the chest, and then transmitted down to the abdomen, is absolutely typical of a dissecting aneurysm of the aorta and would not fit with a coronary occlusion. In the latter, the pain is more localized and if it is felt in the neck, it is usually as a transmission from the precordium, and then it is not transmitted to the abdomen. Here are two types of radiation of precordial pain and they are very seldom combined; on the contrary, in most cases of dissecting aneurysm, the pain starts in the neck, then radiates toward the chest, and then downward toward the abdomen and the legs.

The patient was a hypertensive. We know that dissecting aneurysms occur more often in hypertensive people than in others, and more often in people with atherosclerosis of the aorta. On the contrary, they are not common in luetic patients. If they are present in luetic patients, it is because there is also atherosclerosis of the aorta in addition to the specific lesion. In the differential diagnosis with coronary occlusion, we should keep this in mind: when the pain occurs near the origin of the aorta, there may be a compression of one or both coronary arteries by the extravasated blood; in such cases, the pain may assume the character of coronary pain and the electrocardiogram may show changes which may lead to the diagnosis of coronary occlusion. This is why we are fortunate to have a normal electrocardiogram, so that we can exclude that. However, this is not against dissecting aneurysm because the compression of the coronaries may not take place.

What about the murmurs which were heard in this case? Apparently those heard at the apex are due to transmission of the murmurs from the base, namely, a systolic and an early diastolic murmur. We have no way of knowing whether the patient had murmurs before the last examination. However, I would like to point out that whenever a tear of the aorta occurs not far above one of the leaflets of the aortic valve, this leaflet loses its support and this leads to aortic insufficiency. As a matter of fact, it is typical to describe a diastolic murmur as the result of a tear which takes place at the origin of the aorta.

Some cardiologists admit that there is no aortic insufficiency due to atherosclerosis or fibrosis of the valves. They say that there are three types: the luetic, the endocarditic, and a third type which is seen in older people as a result of incomplete rupture of the aorta. In other words, the aortic insufficiency which was described in older people and was attributed to atherosclerosis, would be due to incomplete rupture of the aorta. I think that these cardiologists go too far, that there still is the possibility of an atherosclerotic type of aortic insufficiency, even though an incomplete rupture followed by healing is more common.

This patient has several symptoms which are neurological in type, so the possibilities are several. One, mentioned by Dr. Freilich, is the compression of one of the carotid arteries by the extrava-

sated blood. Another possibility is the following: the patient had atherosclerosis and arteriosclerosis of the brain arteries. The attack probably caused a drop of blood pressure which went down to 130 when it was recorded, but it dropped even further when the blood pressure was not taken because there was a time when the pulse was not felt. This drop of blood pressure added to the existing arteriosclerosis, and may have precipitated a cerebral thrombosis with softening of the brain tissue. The fact that the reflexes first became weaker and then were exaggerated and that there were changes of the skin color should be attributed to two phenomena: one is the compression of the abdominal aorta by the extravasated blood; the second is the series of neurological phenomena which followed.

The whole syndrome in my opinion, could be explained on the basis of atherosclerosis plus hypertension. I don't think that the patient was a luetic. Apart from atherosclerotic and hypertensive people, rupture of the aorta or dissecting aneurysm is not rare in younger people, usually pregnant women, who present acute abnormalities of the aortic wall on account of disturbances in the metabolism of cholesterol. I don't need to remind you that rupture of the aorta may lead to formation of a dissecting aneurysm.

An aneurysm of this kind may recanalize; there will be a second rupture at a lower level. Then a double circulation is formed: the blood that circulates into the lumen and the blood that circulates between the layers of the aorta and then back into the lumen. In such cases there may be a long survival. There have been cases of this type who survived for 6 months or even one year, and then died of a second rupture. In conclusion, we should admit the formation of a dissecting aneurysm.

Dr. L. Feldman: We had a case at the Cook County Hospital of a colored patient, 45 years old, who gave a similar history. He developed sudden severe pain in the episternal notch while playing cards. We found a moderate hypertension, a systolic thrill in the episternal notch and a diastolic murmur at the aorta area. He denied a luetic infection. It was felt that he had a dissecting aneurysm of the aorta. Two days later he died suddenly, and the autopsy corroborated the diagnosis.

I wish to say one thing about shock, for the benefit of the younger men here. One sees shock in some cases of dissecting aneurysm, just as in myocardial infarction. Such cases have been reported; thus it is not a valid differential point.

When the dissection extends down towards the origin of the coronary arteries, the extravasated blood may compromise these vessels, and EKG change may occur, as Dr. Luisada mentioned. But the changes can be easily differentiated from those of acute coronary occlusion, since there are no ST changes, but just inversion of the T waves, as a result of the cardiac ischemia. Recently a number of such cases appeared in the English literature, holding to the view that such compromise to the coronaries seldom, if ever, gives myocardial infarction. Regarding pregnant women having medial necrosis because of some metabolism disturbance, as mentioned by Dr. Luisada, I wish to add that some of these cases usually have also some congenital deformity of the aorta, as mild coarctation, hypoplasia, etc.

Dr. Luisada: First I want to answer Dr. Feldman about the electrocardiographic changes. It is true that usually they consist of signs of ischemia, but there are reported cases where the dissecting aneurysm was the beginning of a picture which resulted in myocardial infarction. I remember well such a case which was published in the New England Journal of Medicine a few years ago. To get those changes, you must rule out the pericarditis which very often occurs, too.

The coronary arteries are side branches of the aorta. They may become narrow, have a decreased blood flow, or become occluded. They may cause sudden or gradual changes. As far as the aorta is concerned, if you have a tear of the wall, you have an acute onset. You cannot have a gradual onset. The present interpretation is that the initial tear takes place in the media; then the intima in-

vaginates into that and causes the sudden onset of the picture. I think that Dr. Leroy would be better able to handle that than I am. I would not be surprised if there were some cases in private practice which are not recognized. I remember a patient of mine who had atherosclerosis of the aorta and a diastolic murmur. He had a terrific attack of pain, a complete disappearance of the pulse in the right carotid and the right brachial arteries. I made the diagnosis of incomplete rupture of the aorta but I was not able to secure a post mortem.

Dr. N. I. Fox: There is a history of an ulcer here, and according to the history, the ulcer was not found. Occasionally you may have an ulcer of the esophagus, and if that ulcer should rupture, you get immediate stenosis.

PATHOLOGIC REPORT

Dr. Leroy: When the chest cavity was opened, a greatly distended pericardial sac was found, containing about 500 cc. of clotted blood and bloody fluid. (Fig. 1) At 2 cm. above the sinus of Valsalva there was an oblique intimal tear in the ascending aorta measuring 2.5 cm. in length. From that tear blood had dissected the wall of the ascending aorta (Fig. 2) and was clotted in the space between the two layers. There was no connection between the space and the pericardial sac. It seemed that the blood, after dissecting the aortic wall, oozed slowly into the pericardial sac. The blood from this tear had also infiltrated the posterior wall of the heart, thus accounting for subepicardial hemorrhage around the right coronary artery and for the extensive interstitial hemorrhage in the epicardial fat. The blood apparently rushed through the entire wall of the aorta, splitting the wall. This plane of dissection extended into the left coronary artery and also into the peripheral vessels (Fig. 3). It extended into the right common carotid for a distance of 1 cm., 2 cm. into the left renal artery, 1 cm. into the right renal artery, and 9 cm. into the left iliac artery. The other peripheral arteries were all patent. There was moderate atheromatosis of the descending aorta. In spite of the involvement of the renal arteries by this dissecting aneurysm there was no infarction of the kidney. Close examination of the aortic cusp and ascending aorta showed no evidence of syphilis nor of severe atheromatosis. The location of the tear in this case of dissecting aneurysm is characteristic. That area is not usually involved by atheromatous process.

Microscopic study of the aorta and arteries involved by the dissecting aneurysm with the use of special stains (elastica stains and periodic acid stains) revealed the split to occur mainly in the outer third of the media. (Fig. 5.) Near the site of the rupture there was extensive hemorrhagic necrosis in the media with filling of the split with fibrin and blood. The media adjacent to the split revealed the cells to be widely separated by a pink material. This change in the media is regarded by some as a mucoid degeneration and by others as a cystic degeneration. The intima was moderately thickened with splitting in some parts of the internal elastic lamina. The dissection of the aortic wall was irregular in that bands of medial tissue across the split were present in some areas. (Fig. 6). Therefore, dissecting aneurysm is not only a mechanical phenomenon due to the pressure of blood through the vessel walls. It appears to be definitely correlated with a disease of the media of the vessel involved.

The lesions in various parenchymatous organs were secondary to changes in the main blood supply.

In the heart the left coronary artery showed partial dissection of the wall with definite narrowing of the lumen, which was crescent-shaped. (Fig. 7). The media of this vessel demonstrated edema with separation of some of the fibers by pale pink material. Because of narrowing of the lumen of the left coronary artery, a definite partial occlusion of this vessel might be postulated. However, close examination of the heart, mainly the ventricular portion, failed to reveal any gross evidence of recent infarction. In the right auricular wall there was extensive interstitial hemorrhage, extending also into the epicardium. The connective tissue around the right coronary

artery was edematous and contained extravasated blood. The arterioles of the myocardium presented a hyperplastic type of sclerosis with pronounced thickening of the wall. The heart itself was greatly hypertrophied, weighing 550 Gm. From this fact one might infer a history of a long-standing hypertension, usually the rule in cases of dissecting aneurysm.

There were additional changes in the great vessels of the aortic arch. After involving the left coronary artery proximal to the tear, the dissection extended into the right carotid artery, involving a segment 3-4 cm. in length. (Fig. 1).

Therefore, one would expect to find lesions in the brain. Such lesions were demonstrated. There was a well-localized extensive hemorrhagic necrosis of the right basal ganglia, destroying the internal capsule. (Fig. 4). There were also confluent pin-head sized hemorrhages in the cerebral cortex at the base of the right frontal, right temporal, and right parietal lobes. The entire right cerebral hemisphere was extremely enlarged because of edema. The right lateral ventricle was compressed, but there was no blood in the ventricular cavity nor any rupture into the ventricles from the areas of hemorrhage. Microscopic study revealed severe congestion associated with extravasation of blood in perivascular locations. There were also areas of acute necrosis in the brain, secondary to vascular changes, with cystic degeneration and extensive polymorphonuclear infiltration.

In the peripheral vessels there was dissection of the left iliac artery without similar involvement of the right iliac artery. The latter vessel showed extensive atheromatosis with marked hypertrophy of the intima and with thinning out of the media and adventitia. This is the typical atheromatous change in old patients. By contrast the left iliac artery revealed marked hypertrophy of the media and adventitia without participation of the intima. Between the medial cells there was pinkish material. At the site of splitting of the media there was a myxomatous type of degeneration with widely separated cells. The extreme hypertrophy of the adventitia is felt by some observers to be a compensatory to medial disease. There was no evidence of gangrene of the left leg.

Anatomic Diagnoses: Dissecting aneurysm of the aorta, right innominate, left coronary, left renal, and left iliac arteries. Double left carotid artery. Atherosclerosis of the aorta, right coronary, basilar, and left iliac arteries. Hemopericardium. Hypertrophy (550 GM.) and epicardial interstitial hemorrhage of the heart. Healed primary tuberculosis, emphysema, chronic passive congestion, and focal atelectasis of the lungs. Chronic passive congestion and active miliary tuberculosis of the liver. Acute passive congestion and active miliary tuberculosis of the spleen. Acute passive congestion of the kidneys, pituitary, and brain. Acute hemorrhagic encephalomalacia (right basal ganglia, right frontal, right temporal, and right parietal lobes). Cholesterolosis of the gall bladder. Fibrosis of the thyroid.

Cause of Death: Dissecting aortic aneurysm with hemopericardium and acute hemorrhagic encephalomalacia.

SUMMARY AND DISCUSSION

Regarding the pathogenesis of dissecting aneurysm of the aorta, the opinions are varied. The decision as applying to the case at hand is often difficult, as one is seeing only the end results. From the literature some cases are definitely of inflammatory origin; among them are those of syphilitic origin. A recent report described a case of dissecting aneurysm of the so-called diffuse granulomatous type of aortitis but not secondary to syphilis. Some consider this lesion an idiopathic type of inflammatory change, but others believe that it is merely secondary to splitting of the media, the granulomatous lesions resulting from the extravasated blood in the media. In considering atherosclerosis in general, one must bear in mind not only atherosclerosis involving the large vessels but also the degenerative changes affecting the small vessels, especially the nutrient vessels for the larger vessels, namely the vasa vasorum. Present consensus of opinion is that the vasa vasorum play an important role in the production of

cystic degeneration of the media. Of 12 cases of dissecting aneurysm published from the Michael Reese Hospital seven of them demonstrated diffuse hyperplastic sclerosis of the vasa vasorum. Apparently the resulting chronic ischemia led to the changes observed in the media. The prevailing type of dissecting aneurysm of the aorta in the literature at present seems to be of this type. As far as syphilis is concerned, the lesions in the media are apparently secondary to inflammation in the vasa vasorum. Therefore, in the pathogenesis of the medial lesions in this patient the choice lies between nonspecific disease of the vasa vasorum and syphilis; but atherosclerosis does not play an important role in dissecting aneurysm.

An incidental finding was the presence of small tuberculous lesions in the liver, some of them in the active phase. Older tuberculous lesions were demonstrated in both lung apices, from which there was apparently a recent spread. Whether this had a part in the dissecting aneurysm is not known. However, patients who are allergic to protein may develop widespread lesions in the arterioles, whether of the vasa vasorum, arterioles of the kidneys, or other vessels. These changes are usually acute in type. In this case no acute lesions in the vasa vasorum could be demonstrated although some of them were hyperplastic.

In conclusion, then, the immediate cause of death in this case of dissecting aneurysm rests between cardiac tamponade and extensive cerebral hemorrhage.

Dr. Luisada: I think we shouldn't close without asking ourselves whether something can be done for these patients from the point of view of therapy. At present, the consensus of opinion is that nothing can be done. I remember a case of a colleague in Boston who had a gradual development of a mass in the abdomen which was considered a tumor; they opened the abdomen only to find that it was a dissecting aneurysm of the abdominal aorta. In that case they closed the abdomen without doing anything. However, in a case like that where the mass is localized to a section of the abdominal aorta, one could consider wrapping of the aorta in cellophane; it probably would not be the answer because even if one prevents the complete rupture of the vessel, one could not prevent the diffusion of the splitting of the layers of the aorta with subsequent rupture in other points of the vessel. Still, I think that we should keep in mind these problems. There are cases who survive for several months. If something could be done, it certainly would be of help.

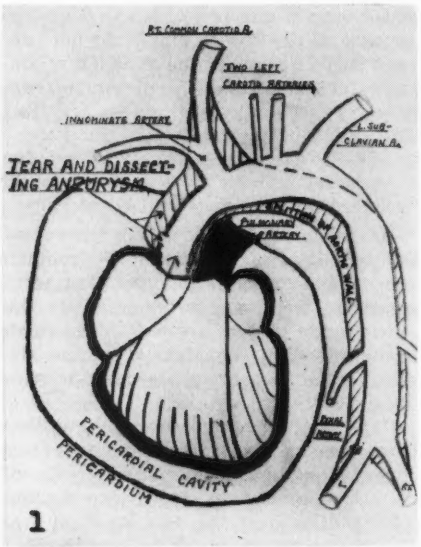
Dr. Leroy: The kidneys failed to reveal any changes on microscopic examination. Apparently the changes that were described were confined mainly to the aorta and larger vessels. The small branches of the renal arteries and the small branches of the coronary arteries were all intact.

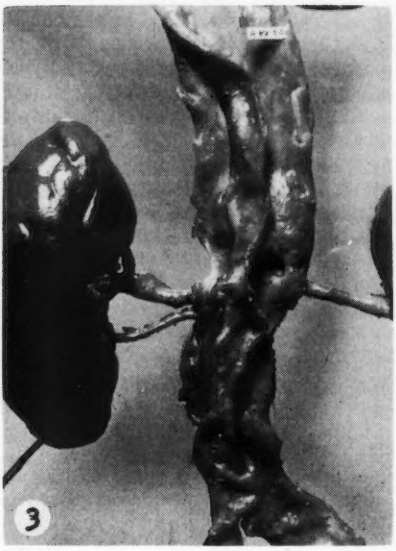
Physician: The purpose of my question is to acquaint myself with the entire theory concerning the pathogenesis of dissecting aneurysm. If we are dealing with a disease of the vasa vasorum, we should see the same thing elsewhere. I would like to know a little more about it.

Dr. Leroy: One must realize that the presence of a localized arteriosclerosis does not necessarily mean that this is due to a lesion in the vasa vasorum and that changes must be present in the arterioles of every single organ. It is well known that a patient may have arteriosclerosis of the kidney without any arteriosclerosis elsewhere. Therefore, I cannot answer your question.

Dr. Feldman: In a case like this where there is hypertension and the hypertension is great in the first portion of the aorta, constant vomiting may increase the pressure considerably. What is the role of hypertension in the pathogenesis of dissecting aneurysm?

Dr. Leroy: The arteriolar changes in hypertension are hyperplastic, but hyalinization of the arteriolar walls soon occurs. It is definitely proven that hypertension has something to do with the pathogenesis of dissecting aneurysm because in the majority of cases reported the blood pressure was above 200 mm. Hg systolic. In one case I can recall, the blood pressure of the patient during life was 290 mm. systolic. At postmortem examination the heart weighed 975 Gm.





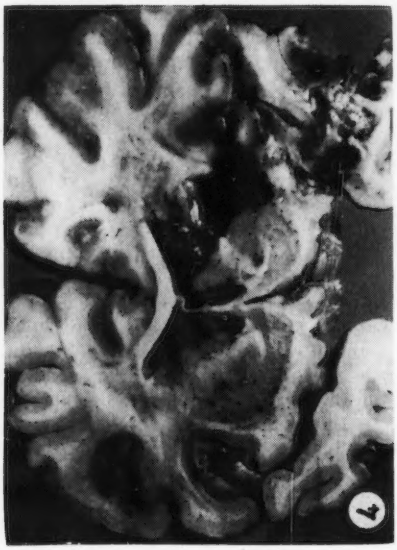


PLATE I

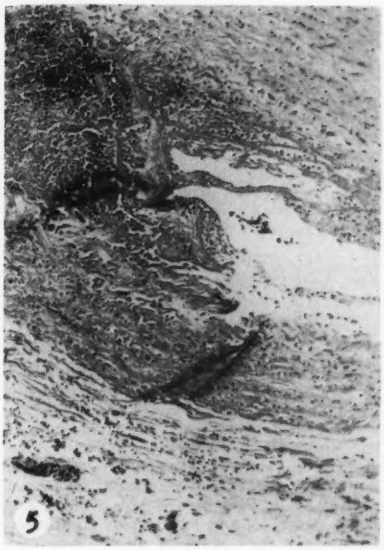
Fig. 1. Diagram of dissecting aneurysm of the aorta.

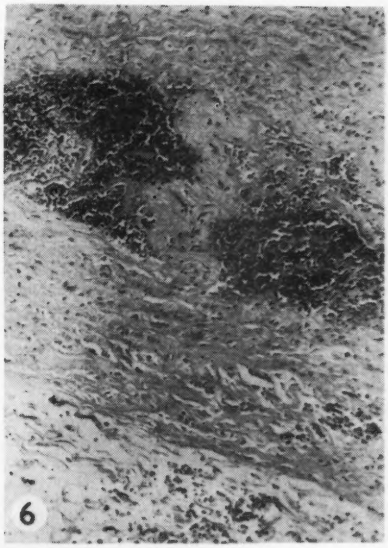
Fig. 2. Ascending aorta: Dissecting aneurysm. The rent seen on the right side of the photograph was the site of entrance for blood from the aorta into the media, causing the latter to be split.

Fig. 3. Abdominal aorta: Dissecting aneurysm. The split in the media of the aorta seen in this photograph also extended into the proximal ends of each renal artery.

Fig. 4. Brain: Coronal section after fixation. In this posterior view there is observed extensive hemorrhage of the right basal ganglia with destruction of the internal capsules as well as hemorrhages in the right temporal area of the cerebrum.

Pictures of Specimens





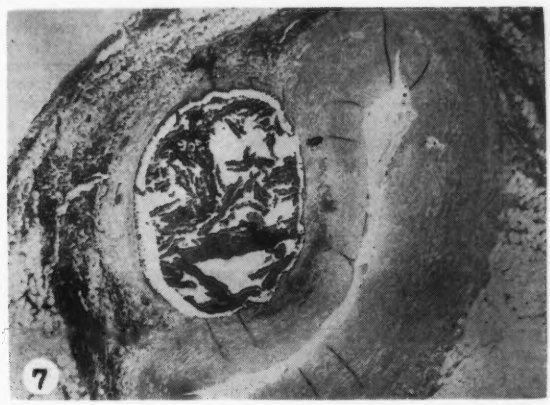


PLATE II

Fig. 5. Aorta: Dissecting aneurysm. The split in the vessel wall occurred mainly in the outer third of the media, with filling of this space formed with fibrin and blood. Photomicrograph x 120.

Fig. 6. Aorta: Dissecting aneurysm. Here the lesion was earlier and incomplete because of the bridge of intact media across the area of splitting. The changes in the media are regarded as either mucoid or cystic degeneration. Photomicrograph x 150.

Fig. 7. Coronary artery: The dissection of the wall in one area produced a narrowing of the lumen, which became crescent shaped. Photomicrograph x 6.

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BOOK REVIEWS

ANATOMY IN SURGERY. By Philip Thorek, M.D., F.A.C.S., F.I.C.S. Cloth 970 pages with 720 figures. Philadelphia, London, Montreal: J. B. Lippincott Company. First Edition, 1951. $22.50.

In this book on surgical anatomy, the author has deviated considerably from the usual plan and has presented the anatomical material with admirable conciseness and completeness with a stronger surgical viewpoint then is usually found in the older texts on surgical anatomy. The entire body is covered in the anatomic discussion and the principles of technic are described for the more important operations. This method of presentation of anatomic data has an obvious advantage in that it correlates the anatomy with the technical phase of surgery. The text is written in a clear and refreshing style. Another attractive feature in this volume is the high caliber of the illustrations—all of which have been drawn by one artist working in close collaboration with the author. The drawings are excellent and are very valuable for their clarity and accuracy. About half of the illustrations are in color—a feature which adds greatly to their value. I believe that this book should be in the library of all surgeons, members of the faculty of anatomy in the medical schools and of all medical students.

PEPTIC ULCER edited by David J. Sandweiss, M.D., F.A.C.P. Cloth. First edition. 790 pages with 164 illustrations. Philadelphia and London: W. B. Saunders Company, 1951. $15.00.

When specialization in medicine was first conceived, it was intended that specialists should devote their efforts to a particular field of medicine so that rapid advances could be made which would then be handed down to the entire medical profession. This book is the superb culmination of just such an endeavor. It is published under the auspices of the American Gastroenterological Association and commendably edited by Dr. Sandweiss. Seventy-seven authorities were selected to contribute, each in the field he seemed best qualified. Every phase of the peptic ulcer problem is discussed. Emphasis is placed upon practical application, but experimental considerations are included and avenues for further research are indicated. The book is very well written and has many excellent illustrations, including roentgenograms. Detailed bibliographies are included for each topic discussed. The book is most highly recommended for gastro-enterologists, surgeons, internists, general practitioners and students.

WOUNDS OF THE EXTREMITIES IN MILITARY SURGERY by Oscar P. Hampton, Jr., M.D., F.A.C.S. Cloth. First edition. 434 pages with 131 illustrations. St. Louis: C. V. Mosby Company, 1951. $10.00.

This new book is intended to serve as a guide for the civilian surgeon entering military surgery. The author has had extensive experience with wounds of the extremities, which constitute some 60% of battlefield injuries. He attempts to orient the surgeon on the management of casualties from the standpoint of materials available, initial, temporary and reparative measures, complications and their prophylaxis and therapy. The more common types of wounds, special types of injury to vessels, nerves, muscles and joints, trench foot and gangrene are all considered in the light of the most accepted forms of treatment. The illustrations are excellent and the legends are extensive and informative. The book is well written. It is recommended for surgeons in the armed forces.

CLINICAL PEDIATRIC UROLOGY by Meredith Campbell, M.S., M.D., F.A.C.S. Cloth. First Edition. 1113 pages with 543 illustrations. Philadelphia and London: W. B. Saunders Company, 1951. $18.00.

This book will undoubtedly become a standard reference text. It is a landmark in the relatively new field of pediatric urology. Every condition is adequately discussed from the standpoints of etiology, pathology, pathogenesis, clinical manifestations, diagnosis, differential diagnosis, treatment and prognosis. Emphasis is placed upon the more common conditions. There are detailed sections dealing with urologic examination and diagnosis and with embryology and anomolies of the genito-urinary tract. Urologic operative procedures are elaborated upon in a section separate from the discussion of the diseases. The discussions are very well illustrated by many clear roentgenograms, photographs of gross and histologic specimens, and excellent line drawings. The author has covered the field comprehensively. He has managed to maintain a lucid style and at the same time include extensive bibliographic material within the text. The book is scholarly, authoritative, and primarily clinical. It is a "must" for urologists, pediatric surgeons and pediatricians. Residents, interns and students will find it excellent for reference purposes.

MEDICAL TREATMENT edited by Geoffrey Evans, M.D., F.R.C.P. Cloth. First edition. 1464 pages with 51 illustrations. London and St. Louis: C. V. Mosby Company, 1951. $20.00.

This book was written in England by 53 contributors. It is arranged alphabetically according to subject, i.e. Cancer, Cardiovascular Disease, Central Nervous System, etc. The disease entities within a subject are also arranged alphabetically, i.e. Skin Diseases: Acne vulgaris, Alopecia, Angiomas, etc. There is, in addition, an excellent 66 page index. This arrangement is very satisfactory for quickly obtaining information about related conditions. Primary concern is given to the medical aspects of therapy, but indications for surgery are cited. The disease manifestations are briefly discussed. Emphasis is placed upon the rationale for each phase of therapy employed, its indications, contraindications and limitations. Practically all fields of medicine are covered. The informa-

tion is presented clearly, concisely and objectively. Bibliographic material, drawn primarily from British and American journals, accompany each section. The book is quite up-to-date and is recommended to internists, general practitioners, interns and medical students as a reference text.

AN ATLAS OF NORMAL RADIOGRAPHIC ANATOMY. By Isadore Meschan, M.A., M.D. Cloth. 593 pages with 362 figures. Philadelphia and London: W. B. Saunders Company. 1951. $15.00.

The present book was undertaken in an effort to make convenient for the practitioner and the specialist a single compendium of normal radiographic anatomy which will include: "(1) basic morbid anatomy as it is applicable to radiography; (2) the manner in which the routine projections employed in radiography are obtained; (3) a concept of the film so obtained; (4) the anatomic parts best visualized on these views; (5) changes with growth and development; and (6) some of the more common variations of normal." In all of these undertakings, Dr. Meschan has succeeded admirably. The book is extremely well written and the radiographs used to illustrate the text are clear and amply serve their assigned functions. The first chapter is used as an introduction to radiography in general and explains the techniques used and the theory used in selecting the different views for the various parts of the body. This book should be in the library of all practitioners and medical students.

ROSENAU'S PREVENTATIVE MEDICINE AND HYGIENE. Edited by Kenneth F. Maxcy, M.D., Ph.D. Cloth. 1462 pages. New York: Appleton-Century-Crofts, Inc. 1951. $14.00.

This seventh edition of the standard text in the field of public health compares favorably with the previous edition and in addition has been enlarged to include most of the modern advances in the fields of preventative medicine and hygiene. Increased attention has been given to the prevention of diseases of non-infectious etiology, to the maitenance of health in middle and old age and to provisions made by the community for treatment and rehabilitation of the sick and of those who are physically or mentally handicapped. The section on Industrial Hygiene has been notably enlarged. The chapter on the effects of radiation has also been expanded to now include the newer material on atomic energy and its public health importance. This book is invaluable to those physicians engaged in public health work and will make an extremely valuable addition to the library of the medical student and practitioner alike.

SURGICAL CARE. By Robert Elman, M.D., F.A.C.S. Cloth. 586 Pages. New York: Appleton-Century-Crofts, Inc. First Edition, 1951. $8.00.

In this book, the author has approached the surgical patient from a rather novel viewpoint. He has ignored the surgical procedure itself and has limited his discussion to the pre- and post-operative care as well as the care of the patient during the actual surgical procedure. Despite the practical approach to the problem, physiologic principles have been constantly emphasized. This book seeks to outline a positive program of surgical convalescence or care that differs from the traditional policy of "letting nature take its course." This book should be in the library of all surgeons, medical school seniors as well as all those physicians who help form part of the "surgical team".

THE SPECIALTIES IN GENERAL PRACTICE. Edited by Russell L. Cecil, M.D. Cloth. 818 pages with 470 figures. Philadelphia & London: W. B. Saunders Company, 1951. $14.50.

Written by 14 contributors, this book is intended as a survey of the specialties for the general practitioner. Rather than discussing the more esoteric and rare diseases, this text discusses in a very lucid manner, the problems which a practitioner is likely to see in his practice. The various procedures discussed are excellently illustrated. This book is to be highly recommended to the practitioner as a general review of the various medical and surgical specialties and to the medical student for a survey of these specialties.

CLINICAL HEART DISEASE. By Samuel A. Levine, M.D. Cloth. 4th edition. 556 pages. 192 figures. Philadelphia & London: W. B. Saunders Company, 1951. $7.75.

Rather than write an exhaustive treatise on Heart Disease, Dr. Levine has presented the field of cardiology from the aspect of the practitioner. While adhering to this viewpoint, the more recent advances in cardiology such as angiocardiography and phonocardiography are discussed. The section on "Clinical Electrocardiography" is very well presented and the various pathologic entities are discussed in relation to the augmented unipolar leads as well as the standard limb leads and chest leads. The chapter on "The Patient with Heart Disease as a Surgical or Obstetric Risk" presents the concept of the patient as an individual with a disease rather than a specific disease occurring in a vacuum. This book is to be highly recommended to all practicing physicians and to all medical students.

ABSTRACTS SECTION

Editor's Note: With this issue we inaugurate a new department—the *Abstracts* section. We will publish abstracts of articles written by members of the faculty and alumni that are published elsewhere in various medical journals. Authors are urged to submit their abstracts as early as possible to The Editor, The Chicago Medical School QUARTERLY, 710 S. Wolcott Ave., Chicago 12, Ill. Abstracts should be between 150-200 words in length. This *Abstracts* section will be a regular feature of the QUARTERLY.

CLARK, GEORGE. Newer Aspects of Frontal Lobe Physiology. Chicago Med. Sch. Quart. No. 30.

Three recent papers were reviewed which make necessary a reexamination of the current theories on frontal lobe functions. In one of these papers it was shown that large frontal removals may be made without the appearance of the usual frontal signs and that such a patient might adjust well within his own group. The second paper transmits the need for reexamination of concepts of cerebral dominance. In the paper it was shown that Broca's speech area may be removed bilaterally with no loss of speech. This paper makes necessary a radical revision of the basic theories of the effects of a frontal lobotomy. It was shown that in a chimpanzee none of the symptoms decided by Jacobson and Fulton (which were the basis for the first lobotomies) may be ascribed to the actual brain removals.

DAVIDSOHN, I., STERN, K., and KASHIWAGI, C.: Mass Blood Grouping and Rh Typing. Am. J. Clin. Path. *21*: 375-386, 1951.

A tentative plan for ABO grouping and Rh typing of blood in a metropolitan area on large numbers of individuals is presented. The desirability of such a plan in operation prior to a disaster situation as well as civilian emergency situations is presented. The objections on the basis of inaccuracies can be overcome if adequate care is observed in technical details.

The plan is possible by employing large numbers of both professional and lay individuals, trained to contribute a specific part of the overall operation. The integration and performance of the personnel is supervised by a trained professional person. The steps involved are drawing of blood, ABO grouping, Rh typing, and correlation of results and labelling. It is estimated that one group of about 10 individuals can type about 150 bloods during a three-hour work period, and in this manner it should be possible to type over one million persons in 10 weeks. The detailed technic and necessary equipment are presented.

GALSTON, BERNARD K. Surgical Evaluation and Management of the Cardiac Patient. Postgraduate Medicine, *10*:2, 1951.

The roles which must be played by the internist, the anesthesiologist and the surgeon in the evaluation and management of the cardiac patient undergoing surgery are discussed. The following facors must be considered by all three before the contemplated surgical procedure is begun: excitement, worry and discomfort, effect of anesthetics on the heart and circulation, peripheral circulatory collapse with the marked alteration in the hemodynamics resulting therefrom, postoperative pain, poor response to infection and tendency to pulmonary embolism and infarction. The internist's chief duties are 1) to determine whether the problem is a surgical one, 2) to determine whether the prognosis of the cardiac condition is good enough to subject the patient to major surgery and 3) to be aware of and familiar with the operative mortality in various cardiac disorders.

The duty of the anesthesiologist is to acquaint himself thoroughly with the cardiac status, the overall physiologic state and particularly the cardiac reserve of the individual patient. The following must be considered: the anesthetic must be safe; induction must be relatively quick so that excitement and struggling may be kept at a minimum; adequate oxygenation must be maintained to combat hypoxia; elimination of CO_2 must be efficient; the working conditions for the surgeon should be satisfactory, and the anesthetist must be skilled and familiar with the management of the anesthetic. Preoperative management, supportive therapy and choice of the anesthetic with an estimation of the various types are all considered.

The role of the surgeon is to insure a minimum of surgical shock, to work as effectively and automatically as possible, as well as to accomplish the surgery for which the patient was brought to the operating room.

Postoperative therapy is reviewed in the manner of present concepts.

The importance of teamwork is stressed, and the various factors influencing the success of the operative procedures are enumerated in detail.

LUISADA, ALDO A. Therapy of Paroxysmal Pulmonary Edema by Antifoaming Agents. Circ., *6*:872, 1950.

Experiments were performed in rabbits in which a series of antifoaming agents were ad-

(Continued on page 96)

SCHOOL NOTES AND NEWS

FACULTY NEWS

The following faculty promotions have been announced by President John J. Sheinin:

Department of Anesthesiology

Dr. Ruth Weyl has been promoted from Assistant Professor to Associate Professor.

Department of Medicine

Dr. Aldo A. Luisada has been promoted from Assistant Professor to Associate Professor.

Dr. Herman L. Eisenberg has been promoted from Instructor to Associate.

Department of Neurology

Dr. Isadore Spinka has been promoted from Associate to Assistant Professor.

Department of Pathology

Dr. Harry Weisberg has been promoted from Research Associate to Assistant Professor.

Department of Pediatrics

Dr. Gordon Cherwitz has been promoted from Instructor to Associate.

Department of Physiology and Pharmacology

Dr. Piero P. Foa has been promoted from Associate Professor to Professor.

Dr. Jay A. Smith has been promoted from Associate to Assistant Professor.

Department of Urology

Dr. David Presman has been promoted from Associate to Assistant Professor.

Department of Medicine

Dr. Luisada, Program Director of Cardiology and Associate Professor of Medicine, has been appointed to the Committee on International Affairs of the American Heart Association, and elected a Fellow of the American Association for the American College of Chest Physicians.

Department of Pathology

Dr. Israel Davidsohn, Professor and Chairman of the Department of Pathology, has been appointed consulting member of the Subcommittee on Blood Grouping Tests of the Committee on Medicolegal Problems of the American Medical Association. Dr. Davidsohn has also been appointed Associate Editor of the American Journal of Clinical Pathology.

Department of Neurology and Psychiatry

Dr. Harry H. Garner, Professor and Chairman of the Department of Neurology and Psychiatry, has recently been appointed to the Illinois State Advisory Committee on Allocation of Mental Health Funds, and also elected a member of the Academy of Forensic Sciences.

Dr. LeRoy P. Levitt has been appointed Consultant in Psychiatry at the Home for Aged Jews in Chicago.

Department of Gynecology

It is with great pleasure that we welcome Dr. William S. Kroger to the faculty of The Chicago Medical School. Dr. Kroger, a graduate of Northwestern University Medical School, is Attending Obstetrician and Gynecologist at Edgewater Hospital and a member of the Courtesy Staff of Chicago Lying-In, and St. Francis Hospital, Evanston. He has been appointed Assistant Professor in the Department.

The Faculty and Alumni Association extend their heartfelt sympathy to the family and friends of Dr. Paul H. Wosika, who died suddenly on September 8, 1951 in the crash of his private plane near Crete, Illinois.

Dr. Wosika, a member of the faculty of The Chicago Medical School since 1942, was Associate Professor in the Department of Medicine and Chairman of the Clinical Promotions Committee of the Faculty. He graduated from the Northwestern Medical School in 1931. He served as Chief of Staff of Illinois Masonic Hospital and was co-author of a text on cardiology and numerous articles concerning various topics in the field.

The untimely demise of Dr. Paul Wosika is a great loss to those of us who have known and worked with him. He will always be remembered as a source of inspiration and guidance to the many students who had the privilege of working with him.

ALUMNI NEWS

Class of 1934

Dr. Louis B. Goldman has been appointed consultant in Proctology at the Manteno State Hospital.

Class of 1939

Dr. Norman W. Jonas is now serving in the Medical Corps of the United States Army.

Class of 1942

Dr. Murray Gutman has recently received his commission in the United States Army Medical Corps.

Class of 1943

Dr. LeRoy P. Levitt, a member of the Faculty of The Chicago Medical School, has recently been certified in Psychiatry by the American Board of Psychiatry and Neurology.

Dr. Victor P. Slepikas has been commissioned a Captain in the United States Army Medical Corps.

Class of 1944

Dr. Bernard K. Galston, associate in Surgery (Anesthesiology) at The Chicago Medical School, has recently been elected a Director of the State of Illinois Anesthesiology Society. Dr. Galston, Head of the Department of Anesthesiology of the Franklin Boulevard Community Hospital and Acting Head of the Department of Anesthesiology at the Chicago Municipal Tuberculosis Sanitarium is also a member of the Chicago Society of Anesthesiologists, a Fellow of the American College of Anesthesiologists and of the International College of Anesthesiologists, and a Fellow of the American College of Chest Physicians.

Dr. Turner Camp is now serving as a member of the United States Navy Medical Corps with the rank of Lieutenant, j.g.

Dr. Milton Wohl has received his commission of Captain in the United States Army Medical Corps.

Class of 1945

Dr. Stanley Friedman, recently commissioned a Captain the United States Army Medical Corps, is now stationed in Japan.

Dr. Marvin B. Rodney has also recently received his commission in the Medical Corps.

Class of 1946

Dr. Sidney Malitz, former Editor-in-Chief of the QUARTERLY, has been granted a leave of absence from the New York State Psychiatric Institute and Hospital where he held the position of Senior Research Psychiatrist to enter the Army as a Captain in the Medical Corps. He was assigned to the Army Medical Center Research and Graduate School at Walter Reed Hospital in Washington, D.C. Dr. Malitz is also a certified examiner in New York State.

Dr. Alan R. Rosenberg is at present stationed overseas as a Captain in the United States Army Medical Corps.

Dr. Eugene J. Rogers is also serving in the United States Army Medical Corps.

Class of 1947

Dr. Frank Rampello has received his commission as First Lieutenant in the United States Army Medical Corps, and is at present stationed at Camp Gordon, Georgia.

Dr. Seymour Warman has also received his commission as First Lieutenant in the United States Army Medical Corps, and is now stationed at Fort Williams, Maine.

Class of 1949

Drs. Abraham H. Rosenstein and Leonard J. Singerman have announced the opening of their office for the practice of General Medicine, Obstetrics, and Minor Surgery in Louisville, Kentucky.

President Sheinin takes pride in announcing that six alumni of the class of 1949, have been certified by the National Board of Medical Examiners during 1950, and are the first group from the school to be so honored. Those certified are Doctors Sheldon G. Altman, Harold Grushkin, Julbert J. Kanter, Seymour H. Kaplan, Jack Margolis and Edward Zucker.

Class of 1950

Dr. Laurence D. Elegant has been appointed Resident in Pediatrics at the Michael Reese Hospital, Chicago.

Dr. Maurice J. Sherman, Jr., has been appointed Resident in Internal Medicine at the Veterans Administration Hospital, Hines, Illinois.

Dr. Leonard Grayson has been appointed a Resident in Dermatology at the Veterans Administration Hospital in Brooklyn, New York. Dr. Grayson has also become the proud father of his second daughter, Elizabeth Marcia, born in July, 1951.

Dr. Nathan Kantor has been appointed a resident in Anesthesiology at the Veterans Administration Hospital in Brooklyn, New York.

Dr. Jerome Litt, former co-editor of The Chicago Medical School QUARTERLY, has been appointed Resident in Dermatology at Kings County Hospital.

Dr. Marvin Wertheim has been appointed Resident in Internal Medicine at the Veterans Administration Hospital in Brooklyn, New York.

Dr. Murray Lieberman has been appointed Resident in Psychiatry at Kings County Hospital in Brooklyn, New York.

Class of 1951

Congratulations to Dr. George Magid on his marriage to the former Miss Jennie Rousso of Seattle, Washington on December 22, 1951.

Best wishes to Dr. and Mrs. Marvin Freedland on the birth of their son, Marvin Bruce.

* * *

The National Board of Medical Examiners announces that Dr. Lawrence Berger made the highest grade in Medicine of the Part II National Board Examinations given in June, 1951. Congratulations, Larry!

Congratulations to Dr. Marvin Freedland who made the highest grade in Public Health of the Part II National Board Examiantion given in June, 1951. These examinations were taken by senior students from all parts of the country.

STUDENT NEWS

Class of 1952

The Office of the Dean has recently announced that Joseph Roshe, of New York City, has attained the highest grade average for the past three years of medical school and ranks first in his class. Mr. Roshe received his A.B. degree from New York University and his M.S. from Northwestern University.

Congratulations to Robert Katz of Brooklyn, New York, on being the recipient of the Junior Scholarship. Mr. Katz received his A.B. from the College of the City of New York.

Best wishes to Herbert Radley on his marriage to the former Miss Charlene Wilder of Chicago, Illinois, on December 23, 1951.

Best wishes to Melvin Levinson on his recent engagement to Miss Joan Shifrin of Chicago.

Congratulations to Burton Krimmer, Managing Editor of The Chicago Medical School QUARTERLY on his engagement to Miss Elaine Brams of Chicago.

Class of 1953

Congratulations to Milton Glickstein of Brooklyn, N. Y., on being awarded the Sophomore Scholarship. Mr. Glickstein received his A.B. degree from New York University.

Class of 1954

Best wishes to Leon Robin on his marriage to the former Miss Eileen Lenit of Chicago on December 23, 1951.

Class of 1955

Congratulations to Burton Zeiger on his engagement to Miss Lenore Kopstein of Chicago, Illinois.

Best wishes to Roy Aimone on his recent engagement to Miss Dorothy Peters of Edna, Texas.

We wish to congratulate Maury Fields on his engagement to Miss Nina Shepard of Brooklyn, New York.

Our best wishes go to Alvin Jackins on his engagement to Miss Arlene Friedman of Bronx, New York.

Congratulations to Burton Blackman on his engagement to Miss Elayne Shwide of Bronx, New York.

Best wishes to Stuart Eichenfeld on his engagement to Miss Frances Fassler of Brooklyn, New York.

We offer congratulations to Seymour Stricker on his marriage to the former Miss Leila Berman of Bronx, New York.

ORGANIZATION NEWS

Phi Delta Epsilon

A Smoker at the Illinois Union on October 12, 1951, was the opening affair of the Beta Tau Chapter of Phi Delta Epsilon for their new members this year. Among the faculty that were there to greet the newcomers were Drs. Eisenstein, Shabat, and Dr. Philip Thorek from the University of Illinois.

A very enjoyable evening was spent by the fraternity at the pledge dance held at the Midland Hotel on Nov. 12. Music, big round tables, and drink-a-plenty helped old and new members to become acquainted. The next dance to be held in February will be in conjunction with the Illinois and Northwestern Chapters of PDE.

The annual Phi D.E. Lectureship was held at Kling Auditorium at Mt. Sinai Hospital in honor of President Sheinin. Dr. Dameshek, a specialist in Hematology, spoke on "Hypersplenism." The talk was thoroughly enjoyed by all.

February 14 will mark another Induction dinner dance for all the Chapters in the Chicago area, as well as alumni of the respective Chapters. As usual, this will be presented at the Furniture Mart, and will be the formal affair of this year.

Phi Lambda Kappa

Our activities for the new school year got off on the right foot with a splendid turnout of potential new members and fraters at the Annual Pledge Meeting held this year in the Parliament Room of the Congress Hotel on Saturday evening, October 6th.

This year we have initiated a new series of lectures by prominent psychiatrists, general practitioners, and sociologists designed to provide useful information to our group and friends concerning problems peculiar to members of the medical profession. These meetings are held once each month in place of one of the usual business meetings. The first two lectures were "The Marital Problems of Medical Students and Physicians" by Dr. A. A. Hilkevitch and "The Doctor and His Children" by Dr. H. Fineberg. Plans have been made to continue this series.

Maurice Laszlo, Editor-in-Chief of The Chicago Medical School QUARTERLY, and Arthur Pinchuck were elected to represent our chapter at the National Convention which was held at the Essex House in NYC during the last week of December. Many of our members from the East had a grand vacation there during the holidays.

Plans are being formulated for an Initiation Dinner, February 10, so that we can allow our new members to participate more fully in our many activities during 1952.

The third Annual Maurice Oppenheim Memorial Lecture will be held on Wednesday, February 6 at 4:00 P.M. at Kling Auditorium of Mount Sinai Hospital. Dr. Charles K. Friedberg of New York will speak on "Recent Advances in the Physiology, Diagnosis and Treatment of Chronic Pulmonary Heart Disease."

Phi Beta Pi

The Beta Mu chapter of the Phi Beta Pi medical fraternity was organized at The Chicago Medical School in the early part of 1949. Dr. L. B. Arey, of Northwestern University, was instrumental in the early formative months of development and in the acceptance of the group into the national organization.

Dr. J. Essenberg and Dr. H. Strong, members of Phi Beta Pi previously, have served ably as faculty advisors from the inception of the group, and recently Dr. J. Smith of the Department of Physiology and Pharmacology has become an honorary member.

At present, we are under the leadership of Gilbert Douglas, and Roland Kowal is the vice-president. Plans for various social and educational activities are under way, one of which is the establishment of an annual lectureship at the school.

Student Council

The Student Council has met three times during the first few weeks of the new school year. The Council has adopted plans for the next twelve months and selected committees to put these plans into effect.

The Student Council consists of nineteen members: two representatives from each class; two from each of the three fraternities; two representatives each from AIMS and the SAMA, and one representative from the QUARTERLY.

In order to complete old business and get new business started on a constructive basis, the Council voted to retain its present officers until January 1, 1952. Present officers are Stuart Cohen, president, Jack Handel, secretary, and Robert Langs, treasurer. A committee, under the chairmanship of Robert Langs, has been formed to publish a directory of faculty and student names and addresses. Since the committee has encountered some difficulty in securing faculty addresses, it may finally emerge as a student directory only.

Reports of student activities are to be turned over to Michael West who will edit and incorporate the information into a Student Council newsletter. The newsletter will be circulated to the student body. A student program committee will apportion days for the activities of various school organizations. A schedule of events for the quarter can be found on the bulletin board in the Student Lounge. A committee headed by Fred Cohen will be concerned with obtaining the best possible health services for CMS students.

Another committee is busily preparing a school-wide social affair. Tentative plans for this event call for an April, 1952 date, though no hotel has as yet been selected. A committee to improve somewhat the physical facilities of CMS is chairmanned by Seymour Kuvin. The commitee's first task will be an effort to constructively transform the Student Lounge into a really comfortable room.

To administer the Oppenheim Fund, a committee headed by Robert Langs has been appointed. Each class is represented by: Walter Kitt, Arthur Pinchuck, Michael West and Charles Weisenthal. Loans from the Fund may be requested by any CMS student. The Council has voted to hold regular meetings the first Thursday of every month. Students are invited to attend and take an active part in the discussions. Attendance at one or two meetings has been spotty and we hope appointed or elected representatives will make every effort to attend future meetings.

Association of Interns and Medical Students

The AIMS chapter of The Chicago Medical School began its 1951 program and membership campaign Oct. 31, 1951, with an address by Dr. Peter Gaberman, Associate Professor of Medicine at The Chicago Medical School. The topic of his talk was "Money and Medicine." An interesting discussion followed the lecture.

The AIMS chapter has been gratified by the response of the student body to its new membership drive. During the past two years our membership has doubled. New elections will be held next quarter.

Our plans for the winter quarter will highlight a seminar on Discrimination. Dr. Falls, Chairman of the Chicago Committee to End Discrimination, will tell us of his experiences with this newly formed organization which AIMS helped form. It has received active support by many medical men, including many men from our own school. This committee closely collaborates with the Mayor's Committee for Better Relations and with the Governor's Committee to End Discrimination.

Another seminar will be devoted to a discussion of the selection of medical students. We hope to have Dean Mullin present since he is vitally interested in this problem. While at the University of Chicago, he worked closely on this problem with Dr. Broson, former Chairman of the Department of Psychiatry at the University of Chicago.

The AIMS Seventeenth Annual Convention which was held Dec. 26-31, 1951, at the Illini Union, was the finest and best attended convention in AIMS' history. Panels on Medical Education, Intern Welfare, Discrimination, Academic Freedom and International Welfare were presented. There also were the usual scientific exhibits.

ABSTRACTS—

(Continued from page 90)

ministered by inhalation in order to decrease the severity of pulmonary edema caused by a standard dose of intravenous adrenaline. Poorly volatile drugs (heavy alcohols, Span 85) failed to exert any favorable effect. Either gave only a slight benefit.

Ethyl alcohol exerted an important favorable action, due to the antifoaming property of alcohol; its action on the central nervous system, though slight because of the small dose used, may have enhanced the effect. The favorable effect of alcohol was comparable to that of morphine. Combination of morphine by injection with alcohol by inhalation gave excellent results, equivalent to those obtained by morphine plus oxygen under pressure.

Experiments were further performed in three other types of experimental pulmonary edema in order to test further the action of alcohol by inhalation.

Pulmonary edema caused by thiourea in the rat was found inconstant and the method was abandoned. Pulmonary edema caused in the guinea pig by ingestion of ammonium chloride proved to lend itself to a therapeutic study. Inhalation of alcohol vapor did not change the average lungs:body ratio. However, this therapy decreased the percentage of animals developing pulmonary edema and improved remarkably the survival time of the animals.

Pulmonary edema caused by rapid intracarotid infusion of physiologic salt solution in the dog can be used only for study of the lungs, as the animals are sacrificed soon after the end of the experiment. Inhalation of alcohol vapor, tried in four animals, gave striking results, entirely preventing the development of pulmonary edema.

Clinical treatment with alcohol by inhalation is now being tried and the results will be reported at a later date.

LUISADA, ALDO A. and MONTES, LUIS PEREZ, A Phonocardiographic Study of Apical Diastolic Murmurs Simulating those of Mitral Stenosis. Ann. Int. Med., *33*:56, 1950.

A clinical and graphic study of apical diastolic murmurs simulating those of mitral stenosis is reported. The study includes cases of mitral insufficiency without appreciable stenosis, aortic insufficiency (Austin Flint murmur), coronary and hypertensive heart disease, adhesive pericarditis, and disturbances of the rate and rhythm.

In a first group of cases, the phonocardiogram revealed that the murmur was not caused by mitral stenosis. This group included cases with arrhythmia, mitral insufficiency, adhesive pericarditis, and some cases of coronary and hypertensive heart disease. In most of these cases, the so-called murmur resulted from an auscultatory illusion and was caused either by a gallop or by a crescendo-type of the first sound.

In a second group of cases, the phonocardiogram revealed diastolic-presystolic vibrations simulating those of mitral stenosis; the functional nature of the murmur was revealed by either the subsequent clinical course or negative postmortem findings. This group included patients with aortic insufficiency (Austin Flint murmur), coronary heart disease, and auricular flutter.

It is concluded that, while the phonocardiogram permits recognition of the nature of the murmur in a large number of cases, it fails to do so in a minority.

The cause of the functional diastolic murmur at the apex is discussed.

SAIDEL, LEO J., GOLDFARB, A. ROBERT, and KALT, WALLACE B.: False Absorption Bands in the Region of 200-230 mu Caused by Stray Radiation in the Beckman Spectrophotometer. Science, June 15, 1951, Vol. 113, No. 2946, pp. 683-685.

Compounds which have a steeply rising absorption with decreasing wavelength in the ultraviolet region from 200-230 mu show a false maximum on the Beckman spectrophotometer. This effect is caused by the increasing amount of stray radiation in the instrument with decreasing wavelength in a region where the transmitted monochromatic radiation is very much less than the transmitted stray radiation. The effect is observed even at low absorbancy values if the solvent absorbs strongly. The details of a procedure for making approximate corrections for the effect of stray radiation in this region are presented, extending the useful range of the instrument.

SMITH, JAY A., and SOHN, HERBERT. The Pressor Effect of Thiamine. Am. Jr. Physiol., (in Press). (Read by title at the Fall Meeting of the Am. Physiol. Soc., September, 1951, Salt Lake City, Utah.)

The first dose of thiamine, 100 mg./kg., causes bradycardia and hypotension; a second similar dose may cause a tachycardia and transitory hypertension, which may be blocked with dibenamine. Tetraethyl ammonium does not interfere with the pressor effect. This is thought to be due to stimulation of sympathetic endings.

SMITH, JAY A., and POST, MELVIN. The Effect of k-Strophanthoside on the Oxygen Consumption of Embryonic Chick Hearts as Measured in the Cartesian Diver. Am. Jr. Physiol., *163*:751, 1950 (abstract).

At a concentration of 1×10^{-6} M, k-strophanthoside causes no change in oxygen consumption, but at 1×10^{-5} M it causes a 5% increase in oxygen consumption of embryonic chick hearts.